

TTW Access DB# 65807 SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: R. GITOMEN Examiner #: 69630 Date: 5/2/02
 Art Unit: 1627 Phone Number 301-8-0732 Serial Number: 09/601,073
 Mail Box and Bldg/Room Location: 3B01 Results Format Preferred (circle): PAPER DISK E-MAIL
7A11

If more than one search is submitted, please prioritize searches in order of need.

 Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____

Earliest Priority Filing Date: _____

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

TTW

John Delaval
 Reference Librarian
 Technology & Chemical Library
 1E07 - 703-308-4498
 delaval@uspto.gov

STAFF USE ONLY		Type of Search	Vendors and cost where applicable
Searcher: <u>Jan</u>	NA Sequence (#) _____	STN <u>✓</u>	
Searcher Phone #: <u>4458</u>	AA Sequence (#) _____	Dialog _____	
Searcher Location: _____	Structure (#) _____	Questel/Orbit _____	
Date Searcher Picked Up: <u>5/13/02</u>	Bibliographic <u>✓</u>	Dr.Link _____	
Date Completed: <u>5/13/02</u>	Litigation _____	Lexis/Nexis _____	
Searcher Prep & Review Time: _____	Fulltext _____	Sequence Systems _____	
Clerical Prep Time: <u>20</u>	Patent Family _____	WWW/Internet _____	
Online Time: <u>+ 85</u>	Other _____	Other (specify) _____	

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 09:33:59 ON 13 MAY 2002

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 - 703-308-4498
ian.delaval@uspto.gov

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 13 May 2002 VOL 136 ISS 20

FILE LAST UPDATED: 10 May 2002 (20020510/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> d all tot

L95 ANSWER 1 OF 28 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:53732 HCAPLUS

DN 132:106966

TI Lupus anticoagulant antibody to F1 region of prothrombin

IN Exner, Thomas; Kraus, Michael

PA Gradipore Limited, Australia; Dade Behring Marburg G.m.b.H.

SO PCT Int. Appl., 17 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07K016-34

ICS C07K016-36; G01N033-86

CC 15-3 (Immunochemistry)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000002925	A1	20000120	WO 1999-AU556	19990709
	W:				
	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,				
	DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,				
	JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,				
	MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,				
	TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,				
	MD, RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,				
	ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,				
	CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9947623	A1	20000201	AU 1999-47623	19990709
	AU 737928	B2	20010906		
	EP 1097174	A1	20010509	EP 1999-930930	19990709
	R:				
	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
	IE, SI, LT, LV, FI, RO				
PRAI	AU 1998-4603	A	19980710		
	WO 1999-AU556	W	19990709		

AB Isolated antibodies directed against the F1 region of **prothrombin**, which antibodies mimic the effect of a **lupus anticoagulant** (LA) in vitro, and uses of the antibodies in **blood clotting tests**.

ST mouse monoclonal antibody human **prothrombin** peptide; **blood clotting test** **lupus anticoagulant** antibody

IT **Venoms**
(Taipan; **lupus anticoagulant**-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting test**)

IT **Bioassay**
(Textarin test; **lupus anticoagulant**-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting test**)

IT **Kaolin, biological studies**
RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study) (**blood clotting time test**; **lupus anticoagulant**-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting test**)

IT **Vipera russelli**
(dil. **Russell's viper venom** time test; **lupus anticoagulant**-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting test**)

IT **Mouse**
Protein sequences
(**lupus anticoagulant**-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting test**)

IT **Antibodies**
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**lupus anticoagulant**-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting test**)

IT **Antibodies**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (**lupus anticoagulants**; **lupus anticoagulant**-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting test**)

IT **Antibodies**
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal; **lupus anticoagulant**-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting test**)

IT **Blood coagulation**
(test; **lupus anticoagulant**-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting test**)

IT 72162-96-0, **Thromboplastin**
RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study) (**activated partial thromboplastin** time test; **lupus anticoagulant**-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting test**)

IT 9035-58-9, **Tissue thromboplastin**

RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study) (inhibition test; lupus anticoagulant-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting** test)

IT 9001-26-7, **Prothrombin**

RL: BSU (Biological study, unclassified); BIOL (Biological study) (lupus anticoagulant-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting** test)

IT 137053-43-1

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study) (lupus anticoagulant-mimicking mouse monoclonal anti-human **prothrombin** F1 region antibodies for **blood clotting** test)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

- (1) Casipit, C; Protein Science 1998, V7, P1671 HCAPLUS
- (2) Exner, T; Thrombosis and Haemostasis 1999, V81(3), P470 HCAPLUS
- (3) Fleck, R; Blood 1988, V72(2), P512 MEDLINE
- (4) Hursting, M; Clinical Chemistry 1993, V39(4), P583 HCAPLUS
- (5) Pelzer, H; Thrombosis and Haemostasis 1991, V65(2), P153 HCAPLUS

L95 ANSWER 2 OF 28 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:621222 HCAPLUS

DN 132:177284

TI Detecting APC-resistant **factor V**: a functional method without **plasma** dilution

AU Rylatt, D. B.; Hohnen-Behrens, C.; Pilgrim, R. L.; Dickeson, L. E.; Neal, M.; Exner, T.

CS Gradipore Research Laboratories, North Ryde, Australia

SO Blood Coagulation & Fibrinolysis (1999), 10(6), 359-366

CODEN: BLFIE7; ISSN: 0957-5235

PB Lippincott Williams & Wilkins

DT Journal

LA English

CC 7-1 (Enzymes)

Section cross-reference(s): 9, 13, 14

AB A method for detecting **activated protein C**

(APC)-resistant **factor V**, esp. **factor**

V Leiden, is described, which uses reagents contg. two unfractionated **snake venoms**. The procedure can be

used for testing **plasma** samples from patients receiving oral **anticoagulant** therapy, **heparin** therapy and patients with

lupus anticoagulant, and does not require the use of

factor-V-deficient plasma. The sample

plasma is first incubated with dil. **venom** from

Agkistrodon contortrix contortrix (Southern

Copperhead) which **activates** the endogenous

protein C and then a dil. **Russell's**

viper venom time test is performed. In individuals with

APC-resistant **factor V**, esp. **factor**

V Leiden, a marginal prolongation of dil.

Russell's viper venom time was noted

[1.14.+-.0.14 s (n = 16)]. Non-carriers were easily discriminated in each patient group, with a prolongation of 2.69.+-.0.30 s for normal

blood donors (n = 127), 2.61.+-.0.38 s for patients taking oral

anticoagulants (n = 102), 2.41.+-.0.45 s for patients taking

heparin (n = 96), and 2.38.+-.0.41 s for patients with **lupus**

anticoagulant (n = 22). Patients taking oral

anticoagulants with moderate prolongation (between 1.5- and

2.0-fold) may have low levels of functional **protein C**

and this might addnl. indicate a subgroup of such patients at higher than normal thrombotic risk.

- ST **blood coagulation factor V**
Leiden assay venom
- IT **Agkistrodon contortrix contortrix**
Anticoagulants
Vipera russelli
(detecting activated protein C-resistant factor V - a functional method without plasma diln.)
- IT Antibodies
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(lupus anticoagulants; detecting activated protein C-resistant factor V - a functional method without plasma diln.)
- IT **Venoms**
(snake; detecting activated protein C-resistant factor V - a functional method without plasma diln.)
- IT **9001-24-5, Blood-coagulation factor V 166799-93-5, Blood-coagulation factor V Leiden**
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(detecting activated protein C-resistant factor V - a functional method without plasma diln.)
- IT **81-81-2, Warfarin 9005-49-6, Heparin, biological studies**
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(detecting activated protein C-resistant factor V - a functional method without plasma diln.)
- IT **42617-41-4, Blood-coagulation factor XIVA**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(detecting activated protein C-resistant factor V - a functional method without plasma diln.)

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Aboud, M; Br J Haematol 1997, V97, P798 MEDLINE
- (2) Bertina, R; Nature 1994, V343, P1534
- (3) Brandt, J; Thromb Haemost 1995, V74, P1185 HCAPLUS
- (4) Chan, W; Blood 1998, V91, P1135 HCAPLUS
- (5) Dahlback, B; Proc Natl Acad Sci USA 1993, V90, P1004 HCAPLUS
- (6) De Ronde, H; Thromb Haemost 1994, V72, P880 HCAPLUS
- (7) Gable, P; Thromb Res 1997, V86, P79 HCAPLUS
- (8) Haas, F; Semin Thromb Haemost 1998, V24, P355 HCAPLUS
- (9) Jorquera, J; Lancet 1994, V344, P1162 MEDLINE
- (10) Kalafatis, M; J Biol Chem 1994, V269, P31869 HCAPLUS
- (11) Kraus, M; Thromb Res 1995, V79, P217 HCAPLUS
- (12) Lewandowski, K; Thromb Res 1997, V85, P105 HCAPLUS
- (13) Reitsma, P; Blood Coag Fibrinol 1996, V7, P659 HCAPLUS
- (14) Ridker, P; N Engl J Med 1995, V332, P912 HCAPLUS

- (15) Robert, A; Thromb Haemost 1996, V75, P562 HCAPLUS
- (16) Shen, L; J Biol Chem 1994, V269, P18735 HCAPLUS
- (17) Svensson, P; Thromb Haemost 1997, V77, P332 HCAPLUS
- (18) Tripodi, A; Thromb Haemost 1997, V77, P436 HCAPLUS
- (19) Van Oerle, R; Am J Clin Path 1997, V107, P521 HCAPLUS
- (20) Van der Meer, F; Thromb Haemost 1997, V78, P631 HCAPLUS
- (21) Williamson, D; Blood 1998, V91, P1140 HCAPLUS
- (22) Zoller, B; J Clin Invest 1994, V94, P2521 MEDLINE

L95 ANSWER 3 OF 28 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:495483 HCAPLUS

DN 131:127393

TI Improved blood coagulation test using whole dilute
Agkistrodon contortrix venom

IN Exner, Thomas

PA Gradipore Limited, Australia

SO PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM G01N033-86

ICS C12Q001-56

CC 9-15 (Biochemical Methods)

Section cross-reference(s): 7, 12

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9939212	A1	19990805	WO 1999-AU69	19990201 <--
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	CA 2318250	AA	19990805	CA 1999-2318250	19990201 <--
	AU 9924041	A1	19990816	AU 1999-24041	19990201 <--
	EP 1068536	A1	20010117	EP 1999-903537	19990201 <--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
	JP 2002502040	T2	20020122	JP 2000-529615	19990201 <--
PRAI	AU 1998-1596	A	19980202	<--	
	WO 1999-AU69	W	19990201	<--	
AB	A method of detg. the coagulation potential of a plasma sample comprising the steps of: (a) preincubating the plasma sample with whole dil. Agkistrodon contortrix venom (ACCV) or like reagent such that (i) endogenous protein C in the plasma is converted into activated protein C by the reagent, and (ii) adding factor Xa which is progressively inactivated by antithrombin III/heparin cofactor (2) during the preincubation; (b) then adding reagents to initiate clotting comprising: (i) an exogenous reagent which activates factor X to Xa or prothrombin to thrombin in a factor V -dependent manner, and (ii) components, such as phospholipid and calcium ions, for efficient coagulation; (c) monitoring a reaction indicative of the rate of coagulation; (d) comparing the rate of coagulation detected in step (b) with the equiv. rate detd. for a normal patient, or comparing the rate of				

coagulation detected in step (b) with the equiv. rate detd. for the plasma sample in the absence of protein C activator; and (e) detg. the coagulation potential of the plasma sample from one or other of the comparisons of step (d). The use of levels of 0.002-0.004% ACCV in the test allows the differentiation between sera from normal individuals from patients with impaired clotting function. Protac from Pentpharm AB did not work very well in the assay.

- ST blood coagulation assay Agkistrodon venom
- IT Phospholipids, biological studies
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(clotting reagent contg.; improved blood coagulation test using whole dil. Agkistrodon contortrix venom)
- IT Blood analysis
Blood coagulation
Blood plasma
Colorimetry
Fluorometry
Surfactants
(improved blood coagulation test using whole dil. Agkistrodon contortrix venom)
- IT Glycosaminoglycans, analysis
RL: ARU (Analytical role, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(in preincubation reagent; improved blood coagulation test using whole dil. Agkistrodon contortrix venom)
- IT Antibodies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(lupus anticoagulants, nonspecific inhibitor, phospholipids to overcome; improved blood coagulation test using whole dil. Agkistrodon contortrix venom)
- IT Detergents
(nonionic; improved blood coagulation test using whole dil. Agkistrodon contortrix venom)
- IT Venoms
(snake, in preincubation reagent; improved blood coagulation test using whole dil. Agkistrodon contortrix venom)
- IT Buffers
Preservatives
(to reverse effect of heparin; improved blood coagulation test using whole dil. Agkistrodon contortrix venom)
- IT Notechis
Notechis scutatus
Oxyuranus scutellatus
Pseudonaja
Pseudonaja textilis
Vipera russelli
(venom, in clotting reagent; improved blood coagulation test using whole dil. Agkistrodon contortrix venom)
- IT Agkistrodon bilineatus
Agkistrodon contortrix
Agkistrodon contortrix laticinctus
Agkistrodon contortrix mokasen
Agkistrodon piscivorus
(venom, in preincubation reagent; improved blood coagulation test using whole dil.

- Agkistrodon contortrix venom)
IT 60202-16-6, Protein C
RL: ARU (Analytical role, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(activation of endogenous, reagent for; improved blood coagulation test using whole dil.
Agkistrodon contortrix venom)
- IT 9001-26-7, Prothrombin 9001-29-0,
Factor X
RL: ARU (Analytical role, unclassified); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(activation of, reagent for; improved blood coagulation test using whole dil. Agkistrodon contortrix venom)
- IT 14127-61-8, Calcium ion, biological studies
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(clotting reagent contg.; improved blood coagulation test using whole dil. Agkistrodon contortrix venom)
- IT 9001-24-5, Blood-coagulation factor
V
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(differentiation of factor V Leiden and; improved blood coagulation test using whole dil.
Agkistrodon contortrix venom)
- IT 166799-93-5, Blood-coagulation factor
V Leiden
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(differentiation of normal factor V and; improved blood coagulation test using whole dil.
Agkistrodon contortrix venom)
- IT 9000-94-6, Antithrombin III
RL: ARU (Analytical role, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(heparin cofactor 2 and, factor Xa in preincubation reagent inactivation by; improved blood coagulation test using whole dil.
Agkistrodon contortrix venom)
- IT 9002-04-4, Thrombin
RL: ARU (Analytical role, unclassified); FMU (Formation, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(improved blood coagulation test using whole dil.
Agkistrodon contortrix venom)
- IT 103469-93-8, Protac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(improved blood coagulation test using whole dil.
Agkistrodon contortrix venom)
- IT 9002-05-5, Factor Xa
RL: ARG (Analytical reagent use); FMU (Formation, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(in preincubation reagent; improved blood coagulation test using whole dil. Agkistrodon contortrix venom)
- IT 9005-49-6, Heparin, analysis 9042-14-2,
Dextran sulfate 75634-40-1, Dermatan

RL: ARU (Analytical role, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(in **preincubation** reagent; improved **blood coagulation** test using whole dil. **Agkistrodon contortrix** venom)

IT 28728-55-4, Polybrene

RL: ARU (Analytical role, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(to reverse effect of **heparin**; improved **blood coagulation** test using whole dil. **Agkistrodon contortrix** venom)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Boehringer Mannheim GmbH; AU 6978587 A 1987
- (2) Gradipore Ltd; AU 3105985 A 1996
- (3) Kabivitrum; WO 9101382 A 1991 HCAPLUS
- (4) Max Plank Ges Wissensch; DE 3724443 A 1989 HCAPLUS
- (5) Ruzicka, K; Thrombosis Research 1997, V87(6), P501 HCAPLUS
- (6) Tripodi, A; Thromb Haemost 1997, V77(3), P436 HCAPLUS

L95 ANSWER 4 OF 28 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:730745 HCAPLUS

DN 130:136228

TI Methods for subtyping lupus **anticoagulants**

AU **Exner, T.**

CS **Gradipore Ltd., Sydney, 2113, Australia**

SO Lupus (1998), 7(Suppl. 2), S103-S106

CODEN: LUPUES; ISSN: 0961-2033

PB Stockton Press

DT Journal

LA English

CC 9-16 (Biochemical Methods)

Section cross-reference(s): 14

AB Two simple procedures were tested for their potential to identify .beta.2-glycoprotein 1 (.beta.2GPI) or **prothrombin** cofactor dependence among lupus **anticoagulants** (LA). The first comprised mixing test **plasma** 1:4 with .beta.2GPI-deficient **plasma** instead of with normal **plasma**. .beta.2GPI deficiency decreased, but did not abolish most LA detectable in KCT, DRVVT and APTT **clotting** tests. Mixing 1:4 with bovine **plasma** was evaluated in a second test based on the KCT in the expectation that **prothrombin**-dependent LA would be preferentially shortened. Bovine **plasma** had a similar correcting effect on LA in all three tests considered here. Conversely, a **prothrombin** antibody was found to have similar prolonging effect on all three of these tests. LA patient **plasmas** displayed considerable heterogeneity when analyzed using a combination of these two tests. The clin. significance of these tests remains uncertain. DRVVT and KCT tests do not appear to discriminate .beta.2GPI-dependent from **prothrombin**-dependent LA.

ST lupus **anticoagulant** subtyping **blood**

coagulation time APTT DRVVT KCT

IT **Blood coagulation**

(**Activated Partial Thromboplastin Time** (APTT), Dil.

Russell Viper Venom Time (DRVVT), Kaolin

Clotting Time (KCT); **blood coagulation**

methods for subtyping lupus **anticoagulants**)

IT Apolipoproteins

RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

(H, .beta.2-glycoprotein 1 dependent lupus **anticoagulant**;

blood coagulation methods for subtyping lupus **anticoagulants**)

IT Blood analysis
 (blood coagulation methods for subtyping lupus anticoagulants)

IT Antibodies
 RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (lupus anticoagulants; blood coagulation methods for subtyping lupus anticoagulants)

IT 9001-26-7, **Prothrombin**
 RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
 (dependent lupus anticoagulant; blood coagulation methods for subtyping lupus anticoagulants)

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
 RE

- (1) Arnout, J; Thromb Haemost 1998, V79, P79 HCAPLUS
- (2) Brandt, J; Thromb Haemost 1995, V74, P1185 HCAPLUS
- (3) Derksen, R; Ann Rheum Dis 1988, V47, P364 MEDLINE
- (4) Exner, T; Br J Haematol 1978, V40, P143 MEDLINE
- (5) Exner, T; Thromb Haemost 1985, V53, P15 MEDLINE
- (6) Galli, M; Blood 1995, V86, P617 HCAPLUS
- (7) Horbach, D; Thromb Haemost 1996, V76, P916 HCAPLUS
- (8) Oosting, J; Thromb Haemost 1992, V67, P499 MEDLINE
- (9) Palosuo, T; Thromb Haemost 1997, V78, P1178 HCAPLUS
- (10) Rao, L; Thromb Haemost 1997, V73, P668
- (11) Smirnov, M; J Clin Invest 1995, V95, P309 MEDLINE
- (12) Takeya, H; J Clin Invest 1997, V99, P2260 HCAPLUS

L95 ANSWER 5 OF 28 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:722802 HCAPLUS

DN 130:195343

TI **Determination of lupus anticoagulant (LA)**

AU Yasumuro, Yoko

CS Department of Clinical Testings, Saint Marianna Medical University, Japan

SO Medical Technology (Tokyo) (1998), 26(10), 1133-1139

CODEN: METCDS; ISSN: 0389-1887

PB Ishiyaku Shuppan

DT Journal; General Review

LA Japanese

CC 15-0 (Immunochemistry)

AB A review with 9 refs. A review with 9 refs. describing the present state of the lupus anticoagulant (LA) or antiphospholipid antibody (aPL) tests. APL antigens comprise **prothrombin**, **.beta.2-glycoprotein 1 (.beta.2GPI)**, **protein C**, **protein S**, and **annexin V**. LA acts as an **anticoagulant** in vitro, but produces **clotting** in vivo. The tissue **thromboplastin** inhibition test (TTI), dild. **activated** partial **thromboplastin** time (dAPTT), kaolin **clotting** time (KCT), dild. **Russell's viper venom** time (DRVVT), platelet neutralization procedure (PNP), and hexagonal (II) phosphatidyl ethanolamine tests for LA are described. The author suggests that low d. phospholipid tests such as TTI or dAPTT should be used for screening, and neutralization tests such as the PNP test, for confirmation. LA testing plays an important role for diagnosis of both **coagulant** diseases (e.g. SLE), and **noncoagulant** diseases, such as cardiac arrest or **thrombosis**.

ST review lupus anticoagulant test diagnosis disease

IT Heart, disease

(arrest; lupus anticoagulant (LA) tests for diagnosis of **coagulant** and **noncoagulant** diseases)

IT Diagnosis

Thrombosis

(lupus **anticoagulant** (LA) tests for diagnosis of **coagulant** and **noncoagulant** diseases)

IT **Antibodies**

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(lupus **anticoagulants**; lupus **anticoagulant** (LA) tests for diagnosis of **coagulant** and **noncoagulant** diseases)

IT **Lupus erythematosus**

(systemic; lupus **anticoagulant** (LA) tests for diagnosis of **coagulant** and **noncoagulant** diseases)

L95 ANSWER 6 OF 28 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:678826 HCAPLUS

DN 130:62727

TI A modified functional **global test** to measure **protein C**, **protein S activities** and the **activated protein C-resistance phenotype**

AU Gemmati, Donato; Serino, Maria L.; Scapoli, Gian L.

CS Centre for the Study of Haemostasis and Thrombosis, University of Ferrara, Ferrara, I-44100, Italy

SO Thrombosis Research (1998), 92(3), 141-148

CODEN: THBRAA; ISSN: 0049-3848

PB Elsevier Science Inc.

DT Journal

LA English

CC 7-1 (Enzymes)

Section cross-reference(s): 14

AB Identifying a defect affecting the **protein C/protein S**

(PC/PS) **anticoagulant** system, using a single global test, has recently become possible thanks to a new methodol. approach based on the **activation** of endogenous **plasma PC** by Protac, derived from **Agkistrodon Contortix snake venom**

(ACV). The introduction of a com. test (ProC Global), ACV-based, provides a useful tool for the screening of **thrombotic** patients since the most frequent causes of inherited **thrombophilia** are found in the PC/PS system. The test provides information only on the global **activity** of the **anticoagulant** pathway but not on PC and PS **activity** or on the **factor V** related conditions (e.g., FV Leiden). The present study shows that by carrying out the test alternating the presence of PC-, PS-, or FV-deficient **plasma** and using appropriate amts. of ACV, it is possible to increase the specificity of the test to correctly evaluate resp. the PC or PS **activities** or the **activated**

protein C resistance condition (APC-R). These simple modifications applied to the original com. test allow to detect exactly, using a single, basic methodol., the principal defects affecting the PC/PS **anticoagulant** pathway. Furthermore, carrying out the tests on an automated **coagulometer**, in combination or not with the classic ProC Global assay, it is possible to use a unique reagent profile to simultaneously investigate in the same or different samples, the PC, PS, and APC-R defect.

ST functional global test **protein C S; activity**
resistance phenotype

IT **Blood-coagulation factors**

RL: ANT (Analyte); ANST (Analytical study)

(protein S; a modified functional global test to measure **protein C**, **protein S activities** and **activated protein C-resistance phenotype**)

IT 9001-24-5, Blood-coagulation factor

V 42617-41-4, Blood coagulation

factor XIVA

RL: ANT (Analyte); ANST (Analytical study)
(a modified functional global test to measure **protein C**, **protein S activities** and **activated protein C-resistance phenotype**)

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

- (1) Amer, L; Thromb Res 1990, V57, P247 MEDLINE
- (2) Dahlback, B; Proc Natl Acad Sci USA 1993, V90, P1004 HCAPLUS
- (3) Dahlback, B; Thromb Res 1995, V77, P1 MEDLINE
- (4) Dati, F; Clin Chem 1997, V43, P1719 HCAPLUS
- (5) Denson, K; S Thromb Res 1996, V81, P151 HCAPLUS
- (6) Faioni, E; Thromb Haemost 1993, V70, P1067 MEDLINE
- (7) Francis, R; Thromb Res 1983, V32, P605 HCAPLUS
- (8) Gemmati, D; Blood Coag Fibrinolysis 1997, V8, P118 MEDLINE
- (9) Gemmati, D; Clin Appl Thromb Hem 1997, V3, P168
- (10) Griffin, J; Blood 1993, V82, P1989 HCAPLUS
- (11) Jorquera, J; Lancet 1995, V344, P1162
- (12) Kraus, M; Thromb Res 1995, V79, P217 HCAPLUS
- (13) Malm, J; Br J Haematol 1988, V68, P437 HCAPLUS
- (14) Nathan, I; Thromb Res 1987, V47, P85 HCAPLUS
- (15) Olivieri, O; Br J Haematol 1995, V91, P465 HCAPLUS
- (16) Ortega, I; Blood Coag Fibrinolysis 1995, V6, P683 HCAPLUS
- (17) Preda, L; Blood Coag Fibrinolysis 1996, V7, P465 HCAPLUS
- (18) Preda, L; S Thromb Res 1990, V60, P19 HCAPLUS
- (19) Robert, A; Thromb Haemost 1996, V75, P562 HCAPLUS
- (20) Solano, C; Blood Coag Fibrinolysis 1997, V8, P268 MEDLINE
- (21) Takahashi, H; Clin Chim Acta 1989, V182, P195 MEDLINE
- (22) Varadi, K; Br J Haematol 1995, V90, P884 HCAPLUS
- (23) Wiesel, M; Thromb Res 1990, V58, P461 MEDLINE
- (24) Wolf, M; Thromb Haemost 1989, V62, P1144 HCAPLUS

L95 ANSWER 7 OF 28 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:557080 HCAPLUS

DN 129:299703

TI Use of **snake venom** fractions in the
coagulation laboratory

AU Marsh, N. A.

CS Research Concentration in Biomedical Science School of Life Sciences,
Queensland University of Technology, Brisbane, QLD 4001, Australia

SO Blood Coagulation Fibrinolysis (1998), 9(5), 395-404
CODEN: BLFIE7; ISSN: 0957-5235

PB Lippincott-Raven Publishers

DT Journal; General Review

LA English

CC 9-0 (Biochemical Methods)

AB A review with 119 refs. **Snake venom** toxins are now regularly used in the **coagulation** lab. for assaying hemostatic parameters and as **coagulation** reagents. **Snake venom thrombin-like enzymes** (SVTLE) are used for fibrinogen and fibrinogen breakdown product assay as well as detecting dysfibrinogenemias. Significantly, because SVTLE are not inhibited by **heparin**, they can be used for defibrinating samples that contain the **anticoagulant** before assay of hemostatic variables. **Prothrombin activators** are found in many **snake venoms** and are used in **prothrombin** assays, for studying **dysprothrombinemias** and prepg. **meizothrombin** and non-enzymic **prothrombin**. **Russell's viper** (*Daboia russelli*) **venom** (RVV) contains a no. of compds. useful in the assay of **factors V, VII, X, platelet factor 3** and **lupus anticoagulants**. **Activators** from the **taipan**, **Australian brown snake** and **saw-scaled viper** have been used to assay **lupus anticoagulants**. **Protein C** and

activated protein C resistance can be measured by means of RVV and Protac, a fast acting inhibitor from Southern copperhead snake venom and von Willebrand factor can be studied with Botrocetin from Bothrops jararaca venom. Finally, phospholipase A2 enzymes and the disintegrins, a family of Arg-Gly-Asp (RGD)-contg. proteins found in snake venoms, show great potential for the study of hemostasis including, notably, platelet glycoprotein receptors GPIIb/IIIa and Ib.

ST review snake venom coagulation

IT Coagulation (blood)

Snake venoms

(use of snake venom fractions in coagulation lab.)

L95 ANSWER 8 OF 28 HCAPLUS COPYRIGHT 2002 ACS

AN 1997:653125 HCAPLUS

DN 127:328522

TI Evaluation of a new screening assay ProC Global for identification of defects in the protein C/protein S anticoagulant pathway

AU Ruzicka, Katharina; Kapiotis, Stylianos; Quehenberger, Peter; Handler, Sylvia; Pabinger-Fasching, Ingrid; Mannhalter, Christine; Jilma, Bernd; Speiser, Wolfgang

CS Clinical Institute of Medical and Chemical Laboratory Diagnostics, University of Vienna, Vienna, A-1090, Austria

SO Thromb. Res. (1997), 87(6), 501-510

CODEN: THBRAA; ISSN: 0049-3848

PB Elsevier

DT Journal

LA English

CC 9-2 (Biochemical Methods)

Section cross-reference(s): 14

AB In the present study a new assay, ProC Global, globally estg. the activity of the main plasma components of anticoagulant protein C/protein S pathway, was evaluated with respect to test characteristics and its sensitivity in the detection of deficiency states of protein C and protein S and of increased activated protein C resistance (aPCR). In the ProC Global assay procedure, protein C is activated in patient's plasma by an activator reagent (venom from Agkistrodon contortrix). The extent of the prolongation of a sample's aPTT, caused by the activation of protein C, is taken as a measure for its anticoagulant capacity. Some 98 patients with one of the above mentioned defects were investigated. Decreased plasma protein C activity and increased aPCR were detected with a sensitivity of 1.0, while only 11 of 14 patients with decreased levels of free protein S antigen showed abnormal results in the ProC Global assay (sensitivity = 0.79). The test can be used in heparinized samples up to 1.0 anti Xa U/mL heparin (UFH and LMWH). When samples from patients on oral anticoagulant treatment are predild. with factor V-deficient plasma the test is sensitive for increased aPCR.

ST anticoagulant screening assay ProC Global; protein C S anticoagulant defect screening; thrombosis
ProC Global screening assay

IT Protein S (blood coagulation factor)

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(-protein C pathway; ProC Global screening assay for identifying defects in protein C/protein S anticoagulant pathway)

IT Coagulation (blood)
 Thromboembolism
 Thrombosis
 (ProC Global screening assay for identifying defects in **protein C/protein S anticoagulant pathway**)

IT Lupus anticoagulant
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (ProC Global screening assay for identifying defects in **protein C/protein S anticoagulant pathway**)

IT Anticoagulants
 (oral; ProC Global screening assay for identifying defects in **protein C/protein S anticoagulant pathway**)

IT 60202-16-6, Protein C
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (-protein S pathway; ProC Global screening assay for identifying defects in **protein C/protein S anticoagulant pathway**)

IT 42617-41-4, Activated protein C
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (ProC Global screening assay for identifying defects in **protein C/protein S anticoagulant pathway**)

L95 ANSWER 9 OF 28 HCAPLUS COPYRIGHT 2002 ACS

AN 1997:132846 HCAPLUS

DN 126:141755

TI Thrombosis risk test

IN Campbell, Paula A.; Preda, Luigi

PA Instrumentation Laboratory, S.P.A., Italy; Campbell, Paula A.; Preda, Luigi

SO PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM G01N033-86

ICS C12Q001-56

CC 9-2 (Biochemical Methods)

Section cross-reference(s): 14

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9642018	A1	19961227	WO 1996-US9036	19960606 <--
W: CA, JP, MX, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5780255	A	19980714	US 1995-488510	19950609 <--
CA 2224465	AA	19961227	CA 1996-2224465	19960606 <--
EP 830608	A1	19980325	EP 1996-919107	19960606 <--
EP 830608	B1	20001004		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE				
JP 11504718	T2	19990427	JP 1996-503149	19960606 <--
AT 196804	E	20001015	AT 1996-919107	19960606 <--
ES 2152531	T3	20010201	ES 1996-919107	19960606 <--
JP 3248621	B2	20020121	JP 1997-503149	19960606 <--
PRAI US 1995-488510	A	19950609 <--		
WO 1996-US9036	W	19960606 <--		

AB The method involves detg. the activity of **protein C** and **protein S** in the **plasma** of an individual thought to be at **thrombotic risk** by adding to a **plasma sample** obtained from the individual: (1) a first reagent in an amt. sufficient to induce or **activate coagulation** in the **plasma**, (2) a second reagent which **activates** endogenous

protein C in the plasma, and (3) a third reagent comprising calcium salts, phospholipids or tissue thromboplastin, or a combination thereof. To a second plasma sample from the same subject is added a reagent which induces or activates coagulation, and a buffer or other material which does not activate protein C, and a third reagent as described above. The time, rate or both necessary for the conversion of endogenous fibrinogen to fibrin in both the first and second samples is measured. The same steps are performed on normal control plasma, and the difference or ratio in the times, rates, or both obtained above are detd. The difference or ratio is indicative of the thrombotic risk in the subject. A kit adapted to carry out the method also is the subject of the present invention. The methods and kits of the invention in other embodiments may comprise a first reagent comprising a synthetic substrate, a second reagent which in the first sample from the subject activates protein C, and in the second sample, a second reagent which does not activate protein C. In these embodiments, the rates of hydrolysis of the synthetic substrates are measured and compared.

- ST thrombosis risk test kit; plasma protein C detn thrombosis risk; protein S detn plasma thrombosis risk
- IT Blood analysis
 Coagulation (blood)
 Thrombosis
 Venoms
 (protein C and protein S detn. in blood plasma in thrombosis risk test)
- IT Protein S (blood coagulation factor)
 RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (protein C and protein S detn. in blood plasma in thrombosis risk test)
- IT Phospholipids, biological studies
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (protein C and protein S detn. in blood plasma in thrombosis risk test)
- IT Fibrins
 RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (protein C and protein S detn. in blood plasma in thrombosis risk test)
- IT Fibrinogens
 RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (protein C and protein S detn. in blood plasma in thrombosis risk test)
- IT Agkistrodon contortrix contortrix
 (venom; protein C and protein S detn. in blood plasma in thrombosis risk test)
- IT 60202-16-6, Protein C
 RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (protein C and protein S detn. in blood plasma in thrombosis risk test)
- IT 7440-70-2D, Calcium, salts 9002-05-5, Factor Xa 9035-58-9, Tissue thromboplastin 37316-87-3, Blood-coagulation Factor IXa
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (protein C and protein S detn. in blood plasma in thrombosis risk test)

L95 ANSWER 10 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 AN 1996:171960 HCAPLUS
 DN 124:197727
 TI Process for the detection of disorders of the **protein C**
 /protein S system
 IN Kraus, Michael
 PA Behringwerke Aktiengesellschaft, Germany
 SO Eur. Pat. Appl., 14 pp.
 CODEN: EPXXDW
 DT Patent
 LA German
 IC ICM C12Q001-56
 CC 9-2 (Biochemical Methods)
 Section cross-reference(s): 13

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 696642	A1	19960214	EP 1995-111554	19950722 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, PT, SE				
	DE 4427785	A1	19960215	DE 1994-4427785	19940808 <--
	CA 2155503	AA	19960209	CA 1995-2155503	19950804 <--
	US 5726028	A	19980310	US 1995-511248	19950804 <--
	AU 9528416	A1	19960222	AU 1995-28416	19950807 <--
	AU 694931	B2	19980806		
	JP 08089293	A2	19960409	JP 1995-200783	19950807 <--
PRAI	DE 1994-4427785		19940808	<--	
AB	A method for detection of disorders of the protein C /protein S system comprising qual. or quant. detn. of functioning of protein C/protein S of the blood coagulation system in a biol. fluid is described. A protein C activator is added to the biol. sample; a contact phase activator is optionally added; the reaction mixt. is incubated ; the coagulation reaction is started by addn. of Ca²⁺ and/or other blood coagulation -inducing agents; and the coagulation activity is detd. The protein C activator is preferably a snake venom enzyme, e.g. those from Agkistrodon . The coagulation activity is measured by detn. of activated , partial thromboplastin time, thromboplastin time, or Russell's viper venom time.				
ST	blood coagulation disorder protein C S; C S protein system defect assay				
IT	Kaolin, analysis RL: ARU (Analytical role, unclassified); ANST (Analytical study) (contact phase activator ; process for detection of disorders of protein C/protein S system)				
IT	Blood coagulation (process for detection of disorders of protein C /protein S system)				
IT	Glass, oxide Phospholipids, analysis RL: ARU (Analytical role, unclassified); ANST (Analytical study) (process for detection of disorders of protein C /protein S system)				
IT	Agkistrodon Agkistrodon contortrix contortrix (protein C activator of venom of; process for detection of disorders of protein C /protein S system)				
IT	Blood-coagulation factors RL: ANT (Analyte); ANST (Analytical study)				

- (protein S, process for detection of disorders of **protein C/protein S system**)
- IT 476-66-4, Ellagic acid 7631-86-9, Silica, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(contact phase **activator**; process for detection of disorders of **protein C/protein S system**)
- IT 60202-16-6, **Protein C**
RL: ANT (Analyte); ANST (Analytical study)
(process for detection of disorders of **protein C** /protein S system)
- IT 7440-70-2, **Calcium**, analysis 9001-24-5, **Blood**
-coagulation factor V 9001-29-0,
Factor X 9035-58-9, **Blood**-
coagulation factor III
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(process for detection of disorders of **protein C** /protein S system)
- L95 ANSWER 11 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:29360 HCAPLUS
DN 124:139313
TI A more discriminating test for APC resistance and a possible
screening test to include **protein C** and
protein S
AU Denson, K. W. E.; Haddon, M. E.; Reed, S. V.; Davidson, S.; Littlewood, T.
J.
CS Thame Thrombosis Haemostasis Research Foundation, Thame, OX9 3NY, UK
SO Thromb. Res. (1996), 81(1), 151-6
CODEN: THBRAA; ISSN: 0049-3848
DT Journal
LA English
CC 7-1 (Enzymes)
Section cross-reference(s): 14
AB The abnormal **activated Protein C** (APC)
cofactor recognized by Dahlback and colleagues, as a cause of APC
resistance, is now known to be due to a mutation in the **Factor**
V mol. resulting in a defect in the APC cofactor, termed
Factor V Leiden. By adding exogenous APC to
an **Activated Partial Thromboplastin Time** (APTT)
reagent, Dahlback introduced the ratio of APC.APTT/ordinary APTT as a
diagnostic test. A ratio of >2.0 indicated normal APC cofactor and a
ratio of <2.0 indicated an APC cofactor defect. Addn. of preformed APC to
plasma, by-passes endogenous **Protein C** (PC)
and Protein S (PS). To characterize the three different defects, PC, PS
and APC cofactor, it is necessary to perform three sep. specific assays as
part of a **thrombophilia** screen. PC in the presence of PS can be
activated to APC by PC **activators** (PCA) either by
thrombin/thrombomodulin, or by **venom** fractions
from a variety of **snakes** including **Agkistrodon**
Contortrix. When PCA is added to **plasma**, the
active inhibitor which destroys **Factors** Va and VIIa, is
generated by endogenous PC, PS and APC cofactor and in the presence of
normal levels of PC and PS, the addn. of PCA to **plasma** will
detect abnormality in the APC cofactor. The advantage of using PCA in the
test system is that it is easier to prep. and standardize, and is more
stable than APC. The authors have investigated the possibility of using
the addn. of PCA instead of APC to **plasma** as a screening test
for the APC inhibitor pathway, and in the presence of normal levels of PC
and PS, as a test for APC resistance.
- ST APC resistance screening **protein C S**
IT Proteins, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)

(a more discriminating test for APC resistance and a possible screening test to include **protein C** and **protein S**)

IT 42617-41-4, **Blood coagulation factor**

XIVa

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(a more discriminating test for APC resistance and a possible screening test to include **protein C** and **protein S**)

L95 ANSWER 12 OF 28 HCAPLUS COPYRIGHT 2002 ACS

AN 1995:780909 HCAPLUS

DN 123:164278

TI Diagnostic methodologies for circulating **anticoagulants**

AU **Exner, Thomas**

CS Haematology Department, Westmead Hospital, Westmead, Australia

SO Thromb. Haemostasis (1995), 74(1), 338-44

CODEN: THHADQ; ISSN: 0340-6245

DT Journal; General Review

LA English

CC 9-0 (Biochemical Methods)

Section cross-reference(s): 14, 15

AB A review with 59 refs. Various types of circulating **anticoagulant** are encountered in **coagulation** testing labs. Those assocd. with bleeding often cause problems in diagnosis. The most common type of acquired **coagulation** inhibitor not assocd. with bleeding is the so-called lupus **anticoagulant** (LA). Differing from systemic lupus erythematosus (SLE) which occurs predominantly in women, primary LA occurs both in females and males. LA are now frequently sought in patients with recurrent fetal losses and acquired **thrombotic** problems as a causative **factor**, whereas in the past they are recorded as a lab. nuisance. Due to the complicating effect of inhibitors on **clotting** tests, diagnosis of various **coagulation** inhibitors remains difficult. There may also be significant overlap between different types of inhibitors. With the recent interest shown in LA, almost all non-specific inhibitors tend to be classed as LA. LA are defined as phospholipid-interfering antibodies. Current criteria have recently been confirmed and include screening with phospholipid-response tests, abnormal mixing studies and correction with phospholipids. However it is becoming clear that even LA as defined may be heterogeneous. Most LA are not directed at neg.-charged phospholipids alone as originally suggested, but rather at complexes of either beta-2-glycoprotein I or **prothrombin** with such phospholipids. There may also be other lipid-assocd. antigens involved. Although earlier work suggests that all LA functioned through a similar mechanism, there is now some preliminary evidence suggesting that various subclasses of LA may account for discrepant results sometimes obtained with different **clotting** tests. A variety of improvements to the basic screening tests for LA (APTT, KCT, DTTI and DRVVT) have recently been suggested. Phospholipid correction or LA-confirmatory tests based on these for the more reliable diagnosis of LA, even in complex clin. conditions have recently become available. Two of the more specific tests for LA recently developed are based on the **factor X activator** from

Russell's viper venom and **prothrombin**

activators from Australian elapid **venoms**.

ST review lupus **anticoagulant** detn diagnosis

IT Antibodies

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(lupus **anticoagulant**; diagnostic methodologies for circulating **anticoagulants** in humans)

IT **Anticoagulants and Antithrombotics**

(lupus-assocd.; diagnostic methodologies for circulating **anticoagulants** in humans)

- L95 ANSWER 13 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:333761 HCAPLUS
DN 122:103382
TI Some recent developments with lupus **anticoagulants**
AU **Exner, T.**
CS Hemostasis Ref. Lab., Westmead hosp., Sydney, 2145, Australia
SO Blood Coagulation Fibrinolysis (1994), 5(2), 281-9
CODEN: BLFIE7; ISSN: 0957-5235
DT Journal; General Review
LA English
CC 15-0 (Immunochemistry)
AB A review with 59 refs. **Lupus anticoagulants (LA)** have been defined as phospholipid-interfering antibodies. Testing for them has become a frequently requested procedure in **coagulation** labs. and new methods have recently become available. **Activated partial thromboplastin time (aPTT)** reagents with reduced levels or different types of phospholipid provide high sensitivity. Correction procedures resistant to **heparin** and based on aPTT and dil. **Russell's viper venom time (DRVVT)** tests with added hexagonal phase phospholipids have improved the specificity of testing. Simplified tests based on **venom activators** of **factor X** and **prothrombin** improve the reliability of LA testing and may facilitate the further categorization of circulating **anticoagulants**. Recent studies on the mechanism of LA derived from various patients have confirmed their heterogeneity, principally in the cofactors involved in their interactions with phospholipids. Perhaps one-third of LA require beta2-glycoprotein 1 to exert an **anticoagulant** effect. The remainder may require human **prothrombin** as suggested from studies with reconstituted **clotting factor** systems.
ST review lupus **anticoagulant** antibody
IT Antibodies
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); ANST (Analytical study); BIOL (Biological study)
(lupus **anticoagulants**, action and detn. and clin. aspects of)
- L95 ANSWER 14 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1993:598160 HCAPLUS
DN 119:198160
TI Evaluation of a new **coagulation** test for **protein C**
AU Kolde, Hans Juergen; Pabinger-Fasching, I.; Darnell, L.; Koder, S.; Simmoteit, R.
CS Baxter Dtschl. G.m.b.H., Unterschleissheim, W-8044, Germany
SO Klin. Labor (1992), 38(12), 665-70
CODEN: KLLAEA
DT Journal
LA German
CC 7-1 (Enzymes)
Section cross-reference(s): 9
AB An automated **coagulation** test for the detn. of **protein C (PC) activity** in human **blood plasma** is described, which is based on the measurement of **activated partial thromboplastin time (aPTT)** prolongation following **activation** with a **PC activator** partially purified from **copperhead snake venom**. Human PC-deficient **plasma** (prepd. by immunoadsorption) was employed to dil. samples and calibrants. Linear calibration curves were obtained between aPPT prolongation and **PC activities** for various mech. or optical **coagulators**; within and between series precisions were 4.5 and 3.3%, resp. Furthermore, the assay discriminated between subjects with hereditary PC deficiency and normal subjects and compared well with other methods for **plasmas** from subjects with or without deficiency and

on oral anticoagulant treatment. Heparin at therapeutic levels did not influence the results.

ST **protein C detn blood coagulation test**

IT **Blood analysis**
(protein C detn. in, of human, coagulation test for)

IT **60202-16-6, Blood coagulation factor XIV**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, in human blood plasma, coagulation test for)

L95 ANSWER 15 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1993:534380 HCAPLUS
DN 119:134380

TI **Methods and kits for determination of protein C using thrombomodulin-thrombin complexes**

IN Funayama, Masashi
PA Funayama Masashi, Japan
SO Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF

DT Patent
LA Japanese
IC ICM C12Q001-56
ICS C12Q001-37
CC 7-1 (Enzymes)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 05130900	A2	19930528	JP 1991-352560	19911111 <--
AB	A method and a kit for detn. of protein C using the immobilized the thrombomodulin-thrombin complex are disclosed. The complex can be immobilized on carriers, e.g., test tubes, beads, filter papers, etc., for activation of protein C prior to assay with conventional methods. The method is more convenient and accurate than the prior arts using snake venom .				
ST	thrombomodulin thrombin complex protein C detn				
IT	Immobilization, biochemical (of thrombomodulin-thrombin complex, for protein C detn.)				
IT	Glycoproteins, specific or class RL: PROC (Process) (thrombomodulins , complexes, with thrombin , immobilization of, for protein C detn.)				
IT	60202-16-6, Protein C RL: ANT (Analyte); ANST (Analytical study) (detn. of, thrombomodulin-thrombin complexes for)				
IT	9002-04-4D, Thrombin, complexes with thrombomodulins RL: PROC (Process) (immobilization of, for protein C detn.)				
IT	139691-92-2, Serine protease inhibitor RL: ANST (Analytical study) (protein C detn. kit contg. thrombomodulin-thrombin complex and)				

L95 ANSWER 16 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1992:168685 HCAPLUS
DN 116:168685

TI A novel **functional assay** of **protein C** in human **plasma** and its **comparison** with amidolytic and **anticoagulant** assays

AU Guglielmone, H. A.; Vides, M. A.

CS Fac. Cienc. Quim., Univ. Nac. Cordoba, Cordoba, 5016, Argent.

SO Thromb. Haemostasis (1992), 67(1), 46-9
CODEN: THHADQ; ISSN: 0340-6245

DT Journal

LA English

CC 7-1 (Enzymes)
Section cross-reference(s): 13

AB A simple and fast method for the quant. detn. of **protein C activity** in **plasma** is here described. The first step consists in the conversion of **protein C** in the test sample into **activated protein C** by means of an **activator** isolated from Southern Copperhead **venom**. Subsequently, the degrdn. of **factor Va**, in presence of **protein C-deficient plasma**, is measured by the prolongation of the **prothrombin** time which is proportional to the amt. of **protein C** in the sample. The dose-response curve showed a linear relationship from 6 to 150% **protein C activity** and the inter- and intra-assay reproducibility was 3.5% and 5.6% resp. In normal subjects, a mean of **protein C** level of 98% of normal pooled **plasma** was found. Comparison with the **anticoagulant** assay in samples of patients with oral **anticoagulant**, liver cirrhosis, disseminated intravascular **coagulation** and severe preeclampsia revealed an excellent correlation ($r = 0.94$, $p < 0.001$). Also, a similar correlation ($r = 0.93$, $p < 0.001$) existed between amidolytic assay and the method here proposed for all the samples studied without including the oral **anticoagulant** group. These results allow the inference that this method evaluates the ability of **protein C** to interact with protein S, phospholipids, **calcium ions** and **factor Va**.

ST **protein C** detn blood analysis human

IT 60202-16-6, **Protein C**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, in blood anal. of human)

L95 ANSWER 17 OF 28 HCAPLUS COPYRIGHT 2002 ACS

AN 1991:602734 HCAPLUS

DN 115:202734

TI Method of determining levels of extrinsic and intrinsic **clotting factors** and **protein C**

IN Carroll, James J.; Autenrieth, Stephen M.

PA Ortho Diagnostic Systems, Inc., USA

SO Eur. Pat. Appl., 18 pp.

CODEN: EPXXDW

DT Patent

LA English

IC ICM G01N033-86

ICS C12Q001-56

CC 9-2 (Biochemical Methods)

Section cross-reference(s): 7

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 434377	A1	19910626	EP 1990-313862	19901218 <--
	EP 434377	B1	19950823		
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
	US 5169786	A	19921208	US 1989-452802	19891219 <--
	CA 2032561	AA	19910620	CA 1990-2032561	19901218 <--
	ES 2088992	T3	19961001	ES 1990-313862	19901218 <--

PRAI US 1989-452802 19891219 <--

AB A method of detg. levels of extrinsic and intrinsic **clotting factors** and **protein C** is provided which is based on the reaction rate of the obsd. **clot** formation and the 1st deriv. of the reaction rate of obsd. **clot** formation. The reaction rate of the obsd. **clot** formation in a **prothrombin** time test or an **activated partial thromboplastin** time assay is detd. for both test and normal **plasma** samples and the reaction rates compared. In another embodiment, the 1st deriv. of the reaction rate of the obsd. **clot** formation is detd. and the results compared. **Clot** signatures for patients with e.g. liver disease, hemophilia, and **protein C** deficiency were detd., as were those for patients undergoing coumarin therapy, etc.

ST **clotting factor** detn **clot** kinetics;
protein C detn **clot** kinetics; **blood coagulation factor** detn **clot** kinetics

IT Hemophilia
Liver, disease or disorder
(clotting factor detn. in, **clot** formation reaction rate in relation to)

IT **Blood-coagulation factors**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, **clot** formation reaction rate in)

IT **Diagnosis**
(extrinsic and intrinsic **clotting factor** and **protein C** detn. for, **clot** formation reaction rate in relation to)

IT **Kinetics, enzymic**
(of **clot** formation, in extrinsic and intrinsic **clotting factor** and **protein C** detn.)

IT **Pharmaceuticals**
(selection of, for patient, extrinsic and intrinsic **clotting factor** and **protein C** detn. for, **clot** formation reaction rate in relation to)

IT **Venoms**
(snake, as **protein C** activator, in **protein C** detn., **clot** formation reaction rate in relation to)

IT **Snake**
(venom of, as **protein C** activator, in **protein C** detn., **clot** formation reaction rate in relation to)

IT 9035-58-9, **Thromboplastin**
RL: ANST (Analytical study)
(activated partial, time, in extrinsic and intrinsic **clotting factor** and **protein C** detn.)

IT 9001-24-5, **Blood-coagulation factor**
V 9001-26-7, **Blood-coagulation factor II** 9001-27-8 9001-28-9, **Blood-coagulation factor IX** 9001-29-0, **Blood-coagulation X** 9001-30-3, **Blood-coagulation factor XII** 9013-55-2, **Blood-coagulation factor XI** 60202-16-6, **Protein C**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, **clot** formation reaction rate in)

IT 91-64-5, **Coumarin** 9005-49-6, **Heparin**, biological studies
RL: ANST (Analytical study)
(therapy with, monitoring of, **blood clotting**)

factor detn. in, clot formation reaction rate in
relation to)

L95 ANSWER 18 OF 28 HCAPLUS COPYRIGHT 2002 ACS

AN 1991:554490 HCAPLUS

DN 115:154490

TI Method and test kit for **protein C** determination using
inactivation of **factors Va** and **VIIIa** by **activated**
protein c

IN Hassouna, Houria I.

PA Michigan State University, USA

SO PCT Int. Appl., 61 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C12Q001-56

ICS G01N033-86

CC 9-2 (Biochemical Methods)

Section cross-reference(s): 7

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9102812	A1	19910307	WO 1990-US4349	19900806 <--
	W: CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
	US 5051357	A	19910924	US 1989-396234	19890821 <--
PRAI	US 1989-396234		19890821 <--		
	US 1989-379988		19890714 <--		
AB	A method and test kit for indirectly detg. protein C are provided. The method uses thrombomodulin/tissue factor and CaCl2 to produce thrombin and activate protein C without fibrin formation, and then allows time for the activated protein C to inactivate coagulation factors Va and VIIIa . A plasma sample deficient in protein C has a decreased activated thromboplastin assay clotting time compared to a control plasma . The method and test kit are useful for diagnosis of thrombic diseases. In addn. to a description of the assay, the issue of substrate specificity for Agkistrodon contortrix contortrix venom , and its protein C-activating component, is addressed. Std. curves for protein C activity are included.				
ST	thrombosis diagnosis protein C detn; protein C detn coagulation factor inactivation; factor Va inactivation protein C detn; VIIIa factor inactivation protein C detn; Agkistrodon venom substrate specificity				
IT	Thrombosis (diagnosis of, protein C detn. method for)				
IT	Venoms (snake, in protein C activation for protein C detn.)				
IT	Blood-coagulation factors RL: ANST (Analytical study) (venom of Agkistrodon contortrix contortrix effect on)				
IT	Agkistrodon contortrix contortrix Snake (venom of, in protein C activation for protein C detn.)				
IT	Glycoproteins , specific or class RL: ANST (Analytical study)				

- (thrombomodulins, in protein C detn.)
- IT 9002-05-5, Thromboplastin
RL: ANST (Analytical study)
(activated, APTT assay, in protein C
detn. by coagulation factors Va and VIIa
inactivation)
- IT 9001-24-5, Blood-coagulation factor
V 9001-27-8
RL: PROC (Process)
(activation of, in protein C detn.)
- IT 9002-04-4, Thrombin
RL: ANST (Analytical study)
(coagulation factors V and VIII
activation by, in protein C detn.)
- IT 42617-41-4, Activated protein C
RL: ANST (Analytical study)
(coagulation factors Va and VIIa inactivation by,
in protein C detn.)
- IT 60202-16-6, Protein C
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, coagulation factors Va and VIIa
inactivation in)
- IT 10043-52-4, Calcium chloride, uses and miscellaneous
RL: USES (Uses)
(in protein C detn.)
- IT 9005-49-6, Heparin, biological studies
RL: BIOL (Biological study)
(protein C detn. in plasma of patient
receiving therapeutic dose of)
- IT 65522-14-7, Blood-coagulation factor Va
72175-66-7
RL: ANST (Analytical study)
(protein C detn. with inactivation of)
- IT 103469-93-8, Protac
RL: ANST (Analytical study)
(substrate specificity of, protein C detn. in
relation to)
- IT 9001-26-7, Prothrombin
RL: ANST (Analytical study)
(time, standardizing, in protein C detn.)
- IT 9001-25-6, Blood-coagulation factor VII
RL: ANST (Analytical study)
(venom of Agkistrodon contortrix
contortrix effect on)
- IT 9001-29-0, Blood-coagulation X
9001-30-3, Blood-coagulation factor XII
RL: ANST (Analytical study)
(venom of Agkistrodon contortrix
contortrix effect on)
- L95 ANSWER 19 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1991:509911 HCAPLUS
DN 115:109911
TI Comparison of test methods for the lupus anticoagulant:
international survey on lupus anticoagulants-I (ISLA-1)
AU Exner, Thomas; Triplett, Douglas A.; Taberner, David A.; Howard,
Margaret A.; Harris, E. Nigel
CS Haematol. Dep., Westmead Hosp., Sydney, Australia
SO Thromb. Haemostasis (1990), 64(3), 478-84
CODEN: THHADQ; ISSN: 0340-6245
DT Journal
LA English
CC 9-15 (Biochemical Methods)

- AB Six lyophilized **plasma** samples were sent to 20 expert labs. for assessment of **lupus anticoagulant** (LA). Four samples contained pooled LA of graded potency mixed with aged normal **plasma**. One contained LA plus cephalin phospholipid and one contained a nonspecific **venom anticoagulant**. Sixteen methods were used overall with some participants using up to 8 methods. Results were scored in regard to the known potencies of LA in the samples and other known induced defects. **Activated partial thromboplastin** time (APTT) tests used by most participants for preliminary screening were relatively sensitive, but nonspecific. Platelet or phospholipid neutralization procedures (PNP) appeared to be sensitive and specific but showed a nonlinear response to increased LA content. Kaolin **clotting** time (KCT) tests showed the most sensitive response to increased LA content but the weaker LA were not scored as abnormal by most labs. as the samples may have contained platelet fragments. Other commonly used tests such as the tissue **thromboplastin** inhibition (TTI) test and the dil. **Russell's viper venom** test (DRVVT) were carried out somewhat inconsistently. The variability in performance of tests in different labs. indicates that standardization of methodol. is urgently required. Generally it seemed that most **clotting** tests were bypassed by the addn. of phospholipid to a known LA-pos. sample in apparently direct proportion to their sensitivity. Sample prepn., esp. prevention of contamination with **activated** platelets is a vital preliminary part in the assay of LA.
- ST **lupus anticoagulant** test method
- IT Lupus erythematosus
(**anticoagulant** in, detn. of, in **blood plasma** of humans, comparison of methods for)
- IT **Blood** analysis
(**lupus anticoagulant** detn. in human, comparison of methods for)
- IT **Anticoagulants** and **Antithrombotics**
(**lupus**, detn. of, in **blood plasma** of humans, comparison of methods for)
- L95 ANSWER 20 OF 28 HCAPLUS COPYRIGHT 2002 ACS
- AN 1989:71533 HCAPLUS
- DN 110:71533
- TI **Functional assays of protein C:**
comparison of two **snake-venom** assays with two **thrombin** assays
- AU Franchi, F.; Tripodi, A.; Valsecchi, C.; Mannucci, P. M.
- CS A. Bianchi Bonomi Hemophilia Thromb. Cent., Univ. Milano, Milan, Italy
- SO Thromb. Haemostasis (1988), 60(2), 145-7
CODEN: THHADQ; ISSN: 0340-6245
- DT Journal
- LA English
- CC 7-1 (Enzymes)
Section cross-reference(s): 14
- AB **Blood-coagulation factor XIV** [**protein C** (PC)] **activities** measured by 2 **thrombin**-based assays have been compared with those obtained by 2 assays based on **snake venom** activation of **plasma PC** followed by measurement of both the amidolytic and **anticoagulant** activities of **activated PC**. This study indicates that **snake venom** assays gave results similar to those of the **thrombin** assays in 20 healthy subjects, in 16 patients with disseminated intravascular **coagulation** disorder, and in 15 patients with congenital PC deficiency. There was, however, some degree of misclassification of normals and congenitally deficient patients, with only the **clotting snake venom** assay resulting in no misclassifications. In 15 patients stabilized on warfarin treatment and

in 17 with liver disease, the **clotting snake venom** assay gave significantly lower values than the other assays, so that it might prove to be more sensitive than the other assays to these defects.

- ST **protein C** detn disease; **blood coagulation factor XIV** detn disease
- IT Liver, disease or disorder
(**blood-coagulation factor XIV** detn. in human in)
- IT **Blood coagulation**
(disorder, disseminated intravascular, **blood-coagulation factor XIV** detn. in human in)
- IT 81-81-2, Warfarin
RL: BIOL (Biological study)
(**blood-coagulation factor XIV** detn. in human in therapy with)
- IT 60202-16-6, **Blood-coagulation factor XIV**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, of human in acquired and congenital deficiencies, comparison of **snake venom** and **thrombin** assays for)
- L95 ANSWER 21 OF 28 HCAPLUS COPYRIGHT 2002 ACS
- AN 1988:545019 HCAPLUS
- DN 109:145019
- TI Fast **functional assay** of **protein C** in whole **plasma** using a **snake venom activator**: evaluation in patients with congenital and acquired **protein C** deficiencies
- AU Takahashi, Hoyo; Hanano, Masaharu; Tatewaki, Wataru; Shibata, Akira
- CS Sch. Med., Niigata Univ., Asahimachi, Japan
- SO Clin. Chim. Acta (1988), 175(3), 217-25
CODEN: CCATAR; ISSN: 0009-8981
- DT Journal
- LA English
- CC 7-1 (Enzymes)
- Section cross-reference(s): 14
- AB Both **anticoagulant** and amidolytic activities of **protein C** (PC) were measured using a **snake venom activator** in patients with hereditary PC deficiency, disseminated intravascular **coagulation** (DIC), and under stabilized warfarin therapy. The results were compared with those obtained by an ELISA. PC levels measured by different functional and immunol. assays were very close in patients with hereditary PC deficiency and DIC. In patients under stable oral **anticoagulant** therapy, there was no detectable difference between amidolytic activity and antigen levels of PC in each patient **plasma**, whereas a decrease in **anticoagulant activity** was much more pronounced. The present activity assays measure PC specifically, and the **snake venom activator** can **activate** both carboxylated and hypocarboxylated forms of PC, but only **anticoagulant** assay can evaluate the physiol. PC function in vitamin K-deficient states.
- ST **plasma protein C** detn disease;
coagulation factor XIV detn **plasma**;
amidolytic assay **protein C** **plasma**;
anticoagulant protein C **plasma**;
immunoassay **protein C** **plasma**
- IT **Agkistrodon contortrix contortrix**
(**protein C** activator of **venom** of, in **protein C** functional activity detn. in human **blood plasma**)

- IT Venoms
(protein C activator of, of
Agkistrodon contortrix contortrix, in
protein C functional activity detn. in
human blood plasma)
- IT Blood coagulation
(disorder, disseminated intravascular,
protein C functional assays in human blood
plasma in, ELISA in relation to)
- IT 60202-16-6, Blood-coagulation factor
XIV
RL: BIOL (Biological study)
(anticoagulant and amidolytic activities of, detn.
of, in human blood plasma in health and disease
with snake venom activator, ELISA in
relation to)
- IT 9001-26-7, Blood-coagulation factor
II 9001-29-0, Blood-coagulation
factor X
RL: BIOL (Biological study)
(of blood plasma of human, protein
C in relation to, in warfarin therapy)
- IT 81-81-2, Warfarin
RL: BIOL (Biological study)
(therapy with, protein C functional assays in human
blood plasma in)
- L95 ANSWER 22 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1988:146143 HCAPLUS
DN 108:146143
TI Characterization and some properties of the protein C
activator from Agkistrodon contortrix
contortrix venom
AU Exner, Thomas; Vaasjoki, Riita
CS Haematol. Dep., Westmead Hosp., Westmead, Australia
SO Thromb. Haemostasis (1988), 59(1), 40-4
CODEN: THHADQ; ISSN: 0340-6245
DT Journal
LA English
CC 7-3 (Enzymes)
Section cross-reference(s): 12
- AB The protein C activator (PCA) detectable in
the venom of A. contortrix contortrix
(Southern copperhead) by specific immunochrometric assay and
anticoagulant activity was isolated and partially
characterized. Chromatog. of the crude venom on SP-Sephadex
followed by Con A Sepharose and finally on hydroxylapatite was necessary
to achieve an electrophoretically pure product. The isolated PCA is a
single-chain glycoprotein with a strong pos. charge and an apparent mol.
wt. of 36,000. It had an immediate inhibitory effect on the
activated partial thromboplastin time (APTT) of normal
plasma with no noticeable effect on the prothrombin
time. Its effect on the APTT was dependent on protein C
and appeared to interfere with the contact mechanism rather than with
factors V and VIII. It had enzymic activity
on some tripeptide chromogenic substrates sensitive to thrombin
and kallikrein. When mixed with normal plasma it generated
activity on substrates sensitive to activated
protein C and should be useful for studies of
protein C.
- ST Agkistrodon venom protein C
activator; snake venom protein
C activator

- IT **Blood-coagulation factors**
RL: BIOL (Biological study)
(protein C activator of Southern
copperhead venom effect on)
- IT **Blood coagulation**
(protein C activator of Southern
copperhead venom inhibition of)
- IT **Agkistrodon contortrix contortrix**
(protein C activator of venom
of, isolation and characterization of)
- IT **Venoms**
(protein C activator of, of Southern
copperhead, isolation and characterization of)
- IT **Kininogens**
RL: BIOL (Biological study)
(high-mol.-wt., protein C activator of
Southern copperhead venom effect on)
- IT **60202-16-6, Blood-coagulation factor
XIV**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(activator, of venom of Southern copperhead
, isolation and characterization of)
- IT **9001-27-8, Blood-coagulation factor VIII,
complex 9001-28-9, Blood-coagulation factor
IX 9001-30-3, Blood-coagulation factor XII
9013-55-2, Blood-coagulation factor XI
9055-02-1, Prekallikrein**
RL: BIOL (Biological study)
(protein C activator of Southern
copperhead venom effect on)
- L95 ANSWER 23 OF 28 HCAPLUS COPYRIGHT 2002 ACS
AN 1987:529568 HCAPLUS
DN 107:129568
TI **Protein C: an automated activity assay**
AU Oedegaard, O. R.; Try, K.; Andersson, T. R.
CS Dep. Clin. Chem., Aker Sykehus, Oslo, Norway
SO Haemostasis (1987), 17(3), 109-13
CODEN: HMTSB7; ISSN: 0301-0147
DT Journal
LA English
CC 7-1 (Enzymes)
Section cross-reference(s): 14
- AB **Protein C in citrated plasma is specifically
activated by the snake venom deriv. Protac,
and the activator is used in a simple, automated assay method.
The activation is completed in <120 s and isolation of
protein C from its inhibitor before activation
is not necessary. The activated protein C
is detd. with the chromogenic substrate S-2366. Therapeutic concns. of
heparin in the test sample do not influence the result. A strong
pos. correlation to immunoassay of protein C is found.
Three cases of probable hereditary protein C
deficiency belonging to the same family were discovered during the study.**
- ST **protein C detn plasma**
- IT **Blood coagulation**
(disorder, protein C deficiency in human)
- IT **60202-16-6, Protein C**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, in human plasma, automated)
- IT **72194-57-1, S-2366 103469-93-8, Protac**
RL: BIOL (Biological study)
(in protein C automated assay, in human

blood plasma)

L95 ANSWER 24 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 AN 1987:435685 HCAPLUS
 DN 107:35685
 TI Quantitative determination of protein C and
 activator preparation for its implementation
 IN Stocker, Kurt F.; Svendsen, Lars G.
 PA Pentapharm A.-G., Switz.
 SO Eur. Pat. Appl., 39 pp.
 CODEN: EPXXDW
 DT Patent
 LA German
 IC ICM C12Q001-38
 ICA C12Q001-56; G01N033-86; A61K035-38; G01N033-68
 CC 7-1 (Enzymes)

Section cross-reference(s): 1

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 203509	A2	19861203	EP 1986-106881	19860521 <--
	EP 203509	A3	19881005		
	EP 203509	B1	19910403		
	R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
	AU 8657369	A1	19861204	AU 1986-57369	19860513 <--
	AU 605462	B2	19910117		
	DK 8602248	A	19861130	DK 1986-2248	19860514 <--
	DK 165199	B	19921019		
	DK 165199	C	19930301		
	IL 78829	A1	19900831	IL 1986-78829	19860519 <--
	AT 62274	E	19910415	AT 1986-106881	19860521 <--
	NO 8602118	A	19861201	NO 1986-2118	19860528 <--
	NO 166303	B	19910318		
	NO 166303	C	19910626		
	ES 555428	A1	19871201	ES 1986-555428	19860528 <--
	CA 1286223	A1	19910716	CA 1986-510137	19860528 <--
	JP 61280298	A2	19861210	JP 1986-122398	19860529 <--
	JP 07036760	B4	19950426		
	ES 557670	A1	19880716	ES 1987-557670	19870814 <--
	ES 557670	A5	19880809		
PRAI	CH 1985-2267		19850529		<--
	CH 1985-4135		19850925		<--
	CH 1985-5087		19851128		<--
	EP 1986-106881		19860521		<--

AB Protein C is detd. in plasma or other samples by activation with snake venom, followed by incubation of the activated protein C (i.e. proteolytically active protein Ca) with a chromogenic oligopeptide substrate R2-D-NHCH[(CH2)NHR3]CO-L-Pro-L-Arg-R1 [R1 = NHC6H3NO2-4, NHC10H7; R2 = H, C2-6 alkanoyl, alkoxycarbonyl, C1-2 alkylsulfonyl, (substituted) benzoyl, (substituted) benzyloxycarbonyl, etc.; R3 = R2, amidino, tosylamidino; n = 3,4] and photometric detn. of the cleavage products. The venom, from Agkistrodon contortix, contains a protein C activator which is useful as an antithrombotic. This activator was purified from venom by chromatog. on DEAE-Sephadex A-50 and used for detn. for protein C in citrated human plasma with D-cyclohexylglycyl-L-prolyl-L-arginine p-nitroanilide-2AcOH as substrate for the protein C2 formed. The protein C activated from venom did not coagulate fibrinogen, did not lyse fibrin, and was not inhibited by antithrombin III, heparin, hirudin, or aprotinin. It had a mol. wt. of about 39,000, and isoelec.

- point of 3.0, and a carbohydrate content of 20%.
- ST **protein C detn plasma; Agkistradon**
venom protein C activator;
snake venom protein C
activator
- IT Peptides, uses and miscellaneous
 RL: USES (Uses)
 (chromogenic, for **protein C detn.**,
activator from snake venom in relation to)
- IT **Agkistrodon contortrix**
Snake
 (protein C activator of venom
 of)
- IT **Venoms**
 (protein C activator of, of snake
)
- IT **Escherichia coli**
 Microorganism
 Saccharomyces cerevisiae
 (protein C detn. in genetically engineered,
activator from snake venom in)
- IT **Animal tissue culture**
 Organ
 (protein C detn. in, activator from
snake venom in)
- IT **Blood analysis**
 (protein C detn. in, of human and other mammals,
activator from snake venom in)
- IT 86890-95-1 88927-41-7 102565-94-6 108963-64-0 108963-66-2
 108963-67-3 108963-68-4 108963-70-8 108963-71-9 108963-72-0
 108963-74-2 108998-14-7
 RL: BIOL (Biological study)
 (as chromogenic substrate, in **protein C detn.**,
activator from snake venom in relation to)
- IT 60202-16-6, **Blood-coagulation factor**
 XIV
 RL: ANT (Analyte); ANST (Analytical study)
 (detn. of, **activator from snake venom** in)
- IT 42617-41-4, **Blood-coagulation factor**
 XIVA
 RL: FORM (Formation, nonpreparative)
 (formation of, **protein C activator** from
snake venom in)
- L95 ANSWER 25 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 AN 1987:191586 HCAPLUS
 DN 106:191586
 TI **Measurement of protein C in plasma**
 - a fully automated assay
- AU McCall, F.; Conkie, J. A.; Walker, I. D.; Davidson, J. F.
 CS Dep. Haematol., R. Infirm., Glasgow, UK
 SO Thromb. Res. (1987), 45(5), 681-5
 CODEN: THBRAA; ISSN: 0049-3848
- DT Journal
 LA English
 CC 7-1 (Enzymes)
 Section cross-reference(s): 1, 14
- AB The assay for vitamin K-dependent **protein C** (**coagulation factor XIV**), which uses a rapid **activator** (Protac C) of **protein C** derived from the **venom** of the **copperhead snake**, was simple and reliable. Using a Gilford 203-S clin. analyzer, the assay was fully automated. It was not subject to the constraints of isolation of

protein C from **plasma** by absorption and elution nor of inhibiting excess **protein C activator**. The assay required only 25 .mu.L test **plasma** and performed at 70 tests/h with good precision and sensitivity; carry-over was within acceptable limits. No **factor Xa** or **thrombin** generation occurred. In both normal controls and untreated patients, good agreement was obtained for **protein C** as detd. by the automated Protac C method and the ELISA procedure. In oral **anticoagulant**-treated patients, however, there was less agreement between the 2 methods as (1) the correlation was lower than that found in the other 2 groups, and (2) **activity** levels of **protein C** were generally lower than the antigen levels (mean values 29% vs. 48%, resp.). Therefore, it seems likely that the method using Protac C **activator** measures only the .gamma.-carboxylated form of **protein C**.

ST **protein C** detn **thrombosis**; **blood coagulation factor XIV** detn automated; Protac C **coagulation factor XIV** detn

IT **Thrombosis**

(**blood-coagulation factor XIV** automated amidolytic detn. in human in)

IT **Anticoagulants and Antithrombotics**

(oral, **blood-coagulation factor**

XIV amidolytic detn. in human **plasma** response to)

IT 60202-16-6, **Blood-coagulation factor XIV**

RL: ANT (Analyte); ANST (Analytical study)

(detn. of, of human **plasma**, fully automated amidolytic)

IT 103469-93-8

RL: BIOL (Biological study)

(in **blood-coagulation factor XIV**

automated amidolytic detn. in human **plasma**)

L95 ANSWER 26 OF 28 HCAPLUS COPYRIGHT 2002 ACS

AN 1986:456677 HCAPLUS

DN 105:56677

TI **Determination of protein C in plasma**

AU Loebermann, H.; Kolde, H. J.; Deubel, R.; Peter, R.; Tourte, E.; Becker, U.

CS Res. Lab., Behringwerke AG, Marburg/Lahn, D-3550, Fed. Rep. Ger.

SO Behring Inst. Mitt. (1986), 79, 112-20

CODEN: BHIMA2; ISSN: 0301-0457

DT Journal

LA English

CC 7-1 (Enzymes)

AB Three new methods to characterize the function of vitamin K-dependent **protein C (blood-coagulation**

factor XIV) in **plasma** are described and

compared to established procedures. Two methods use a **snake**

venom-derived specific **protein C**

activator which allows rapid, sensitive, and standardizable assays

in **plasma** without sample pretreatment. The other technique is

2-dimensional immunoelectrophoresis in the presence of **Ca2+** or

EDTA.

ST **blood coagulation factor XIV** detn

plasma; vitamin K **protein C** detn

plasma

IT 60202-16-6

RL: ANT (Analyte); ANST (Analytical study)

(detn. of, in human **blood plasma**, comparison of methods for)

L95 ANSWER 27 OF 28 HCAPLUS COPYRIGHT 2002 ACS

AN 1986:47533 HCAPLUS
DN 104:47533
TI Detection of specific proenzyme activators in snake
venoms by a new immunoabsorbant-chromogenic substrate
method
AU Exner, Thomas; Cotton, Beth; Howden, Merlin
CS Haematol. Dep., Westmead Hosp., Westmead, NSW 2145, Australia
SO Biochim. Biophys. Acta (1985), 832(3), 351-6
CODEN: BBACAQ; ISSN: 0006-3002
DT Journal
LA English
CC 7-1 (Enzymes)
AB In sep. expts., antibodies to plasminogen, blood-
coagulation factor X, and protein
C were applied to microtiter trays as commonly used in ELISA.
After incubation with dil. normal human plasma as a
source of the corresponding proenzyme antigen, the wells were exposed to
dilns. of various snake venoms. After thorough
washing, the microtiter tray wells were tested overnight with chromogenic
tripeptide substrates known to be relatively specific for the
activated forms of the above factors, i.e., plasmin,
factor Xa, and activated protein
C. The immunochromometric assay described detected 2 new
activators of protein C in Agkistrodon
piscivorus and A. contortrix venoms
and a new factor X activator in A.
rhodostoma venom. Gel filtration of the latter venom
indicated that the factor X activator eluted
with high mol. wt., was clearly distinct from the peak fibrinogen
clotting activity (Ancrod), and appeared to have no
procoagulant activity. Although several Bothrops
venoms appeared to contain plasminogen activator by this
technique, the obsd. strong chromogenic activity was obsd. in
microtiter wells independently of plasminogen and represented nonspecific
amidase activity.
ST proenzyme activator detection snake venom;
Agkistrodon venom proenzyme activator
detection; protein C activator detection
Agkistrodon venom; blood factor
X activator detection Agkistrodon
IT Zymogens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(activators, in snake venom, detection
of)
IT Bothrops
(amidase in venom of, detection of)
IT Agkistrodon rhodostoma
(blood-coagulation factor X
activator in venom of)
IT Snake
(proenzyme activators in venoms of, detection of)
IT Venoms
(proenzyme activators in, of snakes, detection of)
IT Agkistrodon contortrix
Agkistrodon piscivorus
(protein C activator in venom
of)
IT 9001-29-0 60202-16-6
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(activators, in snake venoms, detection
of)
IT 9012-56-0
RL: PROC (Process)

(in venom of Bothrops, detection of)

L95 ANSWER 28 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 AN 1974:459805 HCAPLUS
 DN 81:59805
 TI Biochemical properties of a coagulant enzyme from
Agkistrodon rhodostoma venom
 AU **Exner, Thomas**
 CS Univ. Waterloo, Waterloo, Ont., Can.
 SO (1973) No pp. given Avail.: Natl. Libr. Canada, Ottawa, Ont
 From: Diss. Abstr. Int. B 1974, 34(10), 4817-18
 DT Dissertation
 LA English
 CC 7-2 (Enzymes)
 AB Unavailable
 ST **coagulant enzyme Agkistrodon venom**
 IT Enzymes
 RL: BIOL (Biological study)
 (coagulant, of **Agkistrodon rhodostoma venom**
)
 IT **Venoms**
 (of **Agkistrodon rhodostoma**, coagulant enzyme of)
 IT **Agkistrodon rhodostoma**
 (venom of, coagulant enzyme of)

=> d 163 all

L63 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
 AN 1991:578846 HCAPLUS
 DN 115:178846
 TI Method and kit for determining the endogenous thrombin potential of plasma
 and blood and for pharmaceutical analysis
 IN Hemker, Hendrik Coenraad; Beguin, Suzette Lucette
 PA Neth.
 SO Eur. Pat. Appl., 14 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 IC ICM C12Q001-56
 CC 9-2 (Biochemical Methods)
 Section cross-reference(s): 1, 7

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 420332	A2	19910403	EP 1990-202509	19900921
	EP 420332	A3	19910508		
	EP 420332	B1	19950426		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	NL 8902406	A	19910416	NL 1989-2406	19890927
	AT 121792	E	19950515	AT 1990-202509	19900921
	ES 2072970	T3	19950801	ES 1990-202509	19900921
	JP 03236798	A2	19911022	JP 1990-260273	19900927
	JP 3137261	B2	20010219		
	US 5192689	A	19930309	US 1990-588924	19900927
PRAI	NL 1989-2406	A	19890927		

AB A method for detg. the endogenous thrombin potential (ETP) is described
 which shows how much and for what length of time thrombin has been active
 in a sample of clotting blood or plasma. The ETP can be used for detg.
 the effectiveness of treatment with antithrombotics of any type. The ETP
 detn. comprises adding to the sample a thrombin substrate, an activator of
 thrombin formation, a prepn. of protease inhibitor and, if desired, a
 pharmaceutical for anal. The thrombin substrate is preferably selected to

not completely consume the amt. of thrombin generated in the sample, to have a rate of conversion of the substrate which is proportional to the amt. of thrombin present and to have a measurable conversion product resulting from the conversion by thrombin. Detn. of the amt. of conversion product leads to detn. of the ETP. The choice of activator dets. whether the effect is measured on the intrinsic or extrinsic clotting system, making it possible to det. the effect of the pharmaceutical on various parts of the clotting mechanism. Defibrinated plasma samples contg. various concns. of low-mol. wt. heparin (Fraxiparine) were mixed with buffer contg. CH₃OCO-Gly-Pro-Arg-p-nitroanilide.HCl, thromboplastin, CaCl₂, and antithrombin III. Optical d. at 405 nm was measured 6 min later.

- ST blood thrombin potential detn; pharmaceutical analysis blood thrombin potential
- IT Blood analysis
 - (endogenous thrombin potential detn. in)
- IT Pharmaceutical analysis
 - (endogenous thrombin potential detn. in plasma or blood in)
- IT Anticoagulants and Antithrombotics
 - (endogenous thrombin potential of plasma or blood response to)
- IT Poisons
 - (of Oxyuranus scutellatis, in endogenous thrombin potential detn. in plasma or blood)
- IT Oxyuranus scutellatus
 - (poison of, in endogenous thrombin potential detn. in plasma or blood)
- IT Fibrins
 - RL: ANST (Analytical study)
 - (polymn., inhibition of, in endogenous thrombin potential detn. in plasma or blood)
- IT Spectrochemical analysis
 - (fluorometric, endogenous thrombin potential detn. in plasma or blood by)
- IT Peptides, compounds
 - RL: ANST (Analytical study)
 - (oligo-, arginine-contg., conjugates, with detectable leaving group, as substrate in endogenous thrombin potential detn. of plasma or blood)
- IT Peptides, compounds
 - RL: ANST (Analytical study)
 - (oligo-, conjugates, with detectable leaving group, as substrate in endogenous thrombin potential detn. of plasma or blood)
- IT Spectrochemical analysis
 - (spectrophotometric, endogenous thrombin potential detn. in plasma or blood by)
- IT 9000-94-6, Antithrombin 136535-64-3
 - RL: ANST (Analytical study)
 - (as protease inhibitor in endogenous thrombin potential detn. of plasma or blood)
- IT 901-47-3 60457-00-3, S2222 136552-31-3
 - RL: ANST (Analytical study)
 - (as substrate in endogenous thrombin potential detn. of plasma or blood)
- IT 9002-04-4, Thrombin
 - RL: PRP (Properties)
 - (blood or plasma potential of, detn. of)
- IT 104521-37-1, Fraxiparine
 - RL: ANST (Analytical study)
 - (endogenous thrombin potential of defibrinated plasma response to)
- IT 24967-94-0, Dermatan sulfate 9005-49-6, Heparin, biological studies
 - RL: ANST (Analytical study)
 - (endogenous thrombin potential of plasma or blood response to)
- IT 618-39-3, Benzamidine 9002-05-5, Thromboplastin 136552-32-4
 7440-70-2, Calcium, biological studies 8001-27-2, Hirudin 10043-52-4,
 Calcium chloride, biological studies

RL: ANST (Analytical study)
(in endogenous thrombin potential detn. of plasma or blood)
IT 9001-26-7, Prothrombin
RL: ANST (Analytical study)
(thrombin generation and detn. from, prolonged anticlotting treatment
effect on)

=> d hitstr 163

L63 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
IT 136535-64-3
RL: ANST (Analytical study)
(as protease inhibitor in endogenous thrombin potential detn. of plasma
or blood)
RN 136535-64-3 HCAPLUS
CN Antithrombin, mixt. with heparin cofactor II (9CI) (CA INDEX NAME)

CM 1

CRN 81604-65-1
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 9000-94-6
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> d his

(FILE 'HOME' ENTERED AT 07:32:18 ON 13 MAY 2002)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 07:32:46 ON 13 MAY 2002

E PROTEIN C/CN
L1 1 S E3
E ACTIVATED PROTEIN C/CN
L2 1 S E3
E BLOOD-COAGULATION FOACTOR XA/CN
E BLOOD-COAGULATION FACTOR XA/CN
L3 1 S E3
E ANTITHROMBIN III/CN
L4 1 S E3
E HEPARIN COFACTOR 2/CN
L5 1 S E6
L6 2 S 9000-94-6/CRN
L7 1 S 81604-65-1/CRN
L8 1 S L6 AND L7
E BLOOD-COAGULATION FACTOR X/CN
L9 1 S E3
E PROTHROMBIN/CN
L10 1 S E3
E THROMBIN/CN
L11 1 S E3
E BLOOD-COAGULATION FACTOR V/CN
L12 1 S E3

L13 2 S (HEPARIN OR HEPARIN, SODIUM SALT)/CN
L14 1 S DERMATAN/CN
L15 1 S DEXTRAN SULPHATE/CN

FILE 'HCAPLUS' ENTERED AT 07:39:58 ON 13 MAY 2002

E EXNER T/AU
L16 54 S E3-E5
E GRADIPORE/PA,CS
L17 33 S E3-E18
L18 80 S L16,L17
E OW99-AU69/AP,PRN
E WO99-AU69/AP,PRN
L19 1 S E3,E4
L20 1 S L18 AND L19

FILE 'REGISTRY' ENTERED AT 07:44:29 ON 13 MAY 2002

L21 1 S 14127-61-8
L22 1 S 28728-55-4
L23 1 S 166799-93-5

FILE 'HCAPLUS' ENTERED AT 07:45:52 ON 13 MAY 2002

E VENOM/CW
L24 9457 S E4
E VENOM/CT
E E7+ALL
L25 9273 S E3+NT
L26 19658 S E3,E5/BI
L27 7518 S SNAKE (L) VENOM?
L28 19690 S L24-L27
E AGKISTRODON/CT
E E3+ALL
L29 518 S E6+NT
L30 1268 S E6-E27/BI
E AGKISTRODON
L31 1277 S E1-E14
L32 243 S (AGKISTRO? OR A) () (CONTORTRIX OR PISCOVOR? OR BILINEAT? OR MO
L33 227 S AGKISTRO? (L) (CONTORTRIX OR PISCOVOR? OR BILINEAT? OR MOCCAS
L34 19855 S L28-L33
E VIPER/CT
E E4+ALL
L35 2 S E3,E4
E E28+ALL
L36 262 S E7+NT
L37 369 S E7-E12/BI
E E6+ALL
L38 615 S E6+NT
L39 1124 S E6-E35/BI
E VIPER
L40 2387 S E3,E4,E7,E8,E9,E10,E11
L41 447 S E13-E17,E22,E23,E24
E NOTECHIS/CW
L42 104 S E3
E NOTECHIS/CT
E E3+ALL
L43 104 S E6+NT
L44 162 S E6-E17/BI
E PSEUDONAJA/CT
E E3+ALL
L45 38 S E6+NT
L46 54 S E6-E12/BI
E OXYURANUS/CT
E E5+ALL
L47 77 S E6+NT

L48 122 S E6-E10/BI
 L49 20335 S L34-L48
 L50 976 S RUSSEL?(L) (SNAKE OR VIPER?)
 L51 156 S COPPERHEAD OR COPPER HEAD
 L52 20373 S L49-L51
 L53 11 S L18 AND L52
 E BLOOD COAGULATION/CT
 E E3+ALL
 L54 12573 S E7+NT
 E BLOOD CLOT/CT
 E E6+ALL
 L55 483 S L52 AND L54
 L56 2295 S L52 AND (?COAGUL? OR CLOT?)
 L57 2295 S L55,L56
 L58 168 S L52 AND (L1 OR PROTEIN C OR FACTOR XIV)
 L59 158 S L52 AND (L2 OR PROTEIN C (L) ACTIV? OR FACTOR XIVA)
 L60 157 S L58 AND L59
 L61 42 S L60 AND (L3 OR FACTOR XA OR FACTOR X(L)ACTIV?)
 L62 0 S L60 AND L8
 L63 1 S L8
 L64 1 S L60 AND (L4 OR ANTITHROMBIN III) AND (L5 OR HEPARIN (L) COFAC
 L65 103 S L60 AND (L9 OR FACTOR X OR L10 OR PROTHROMBIN OR FACTOR II OR
 L66 24 S L60 AND (L21 OR CALCIUM(L)ION OR CA2# OR CA(L)ION)
 L67 19 S L60 AND (L13 OR L14 OR L15 OR HEPARIN OR DERMATAN OR DEXTRAN(
 L68 18 S L60 AND (L23 OR FACTOR(L)V (L) LEIDEN)
 L69 76 S L61,L66-L68
 L70 62 S L69 AND L65
 L71 22 S L70 AND 9/SC
 L72 16 S L69 AND BLOOD ANALYSIS/CT
 L73 8 S L71 AND L72
 L74 8 S L73 AND L24-L73
 SEL DN 3 5 6
 L75 5 S L74 NOT E1-E3
 L76 128 S L60 AND (PD<=19980202 OR PRD<=19980202 OR AD<=19980202)
 L77 29 S L76 AND (BIOCHEM?(L)METHOD?)/SC,SX
 L78 26 S L77 AND L61-L75
 L79 68 S L76 AND L61-L75 NOT L77
 L80 17 S L79 AND (SCREENING OR KIT OR FUNCTIONAL ASSAY OR COMPARISON O
 L81 2 S L79 AND PROTAC/TI
 L82 6 S L79 AND BLOOD ANALYSIS/CT
 SEL DN 5 6
 L83 4 S L82 NOT E4-E5
 L84 13 S L80 NOT L81-L83
 SEL DN 3 7 12 13
 L85 9 S L84 NOT E6-E9
 L86 31 S L20,L53,L63,L64,L75,L81,L83,L85
 L87 59 S L69 AND L76
 L88 46 S L87 NOT L86
 SEL DN 4 6 9 15 23 27 28 38 39
 L89 9 S L88 AND E10-E18
 L90 18 S L85,L89
 L91 29 S L53,L90
 L92 29 S L91 AND (?COAGUL? OR CLOT? OR FACTOR OR BLOOD OR PLASMA OR SE
 L93 11 S L91 AND (RUSSEL? OR VIPER? OR PSEUDON? OR TEXTIL? OR NOTECH?
 L94 29 S L92,L93 AND L16-L20,L24-L93
 SEL DN 20
 L95 28 S L94 NOT E19

FILE 'HCAPLUS' ENTERED AT 09:33:59 ON 13 MAY 2002

=> fil biosis

FILE 'BIOSIS' ENTERED AT 09:48:20 ON 13 MAY 2002

COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 8 May 2002 (20020508/ED)

=> d all tot

L109 ANSWER 1 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:61534 BIOSIS
DN **PREV200200061534**
TI Apparatus and method for detecting coagulation in blood samples.
AU **Exner, T.**
CS Gordon Australia
ASSIGNEE: GRADIPORE LIMITED
PI US 5601995 Feb. 11, 1997
SO Official Gazette of the United States Patent and Trademark Office Patents,
(Feb. 11, 1997) Vol. 1195, No. 2, pp. 1164.
ISSN: 0098-1133.
DT **Patent**
LA English
NCL 435013000
CC Blood, Blood-Forming Organs and Body Fluids - General; Methods *15001
Methods, Materials and Apparatus, General - Laboratory Methods *01004
IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Methods and
Techniques
IT Miscellaneous Descriptors
ANALYTICAL TECHNIQUES; BLOOD SAMPLE; COAGULATION; METHODS

L109 ANSWER 2 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:451086 BIOSIS
DN **PREV200000451086**
TI Activated protein C resistance test.
AU **Exner, Thomas (1)**
CS (1) Gordon Australia
ASSIGNEE: Gradipore Limited, North Ryde, Australia
PI US 6051434 April 18, 2000
SO Official Gazette of the United States Patent and Trademark Office Patents,
(Apr. 18, 2000) Vol. 1233, No. 3, pp. No pagination. e-file.
ISSN: 0098-1133.
DT **Patent**
LA English
AB The method for determining functional activity of protein C in a human
plasma sample includes incubating the human plasma sample with exogenous
reagents that activate factor V and a common pathway of the blood
coagulation mechanism through factor X, with activated exogenous protein C
and with components that are necessary for efficient clotting of the human
plasma sample, or incubating the human plasma sample with exogenous
reagents that induce the presence of thrombin in a factor V dependent
manner, with activated exogenous protein C and with components that are
necessary for efficient clotting of the human plasma sample; monitoring a
reaction indicative of a potential rate of coagulation of the plasma
sample and comparing the resulting potential rate of coagulation with an
equivalent rate for normal patient, or comparing the resulting potential
rate of coagulation with an equivalent rate determined for the plasma
sample in the absence of activated exogenous protein C; and determining
the functional activity of the free protein C from this comparison.
NCL 436069000
BC Hominidae 86215

IT Major Concepts
 Biochemistry and Molecular Biophysics; Methods and Techniques; Blood
 and Lymphatics (Transport and Circulation)

IT Parts, Structures, & Systems of Organisms
 plasma: blood and lymphatics

IT Chemicals & Biochemicals
 factor V; factor X; protein C

IT Methods & Equipment
 activated protein C resistance test: analytical method

ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
 human (Hominidae)

ORGN Organism Superterms
 Animals; Chordates; Humans; Mammals; Primates; Vertebrates

RN 9001-29-0 (FACTOR X)
 60202-16-6 (PROTEIN C)

L109 ANSWER 3 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 1999:146080 BIOSIS
 DN PREV199900146080
 TI Methods for subtyping lupus anticoagulants.
 AU Exner, T. (1)
 CS (1) Haemostasis Res. Lab., Gradipore Ltd., PO Box 1865, Macquarie Cent.,
 North Ryde, NSW 2113 Australia
 SO Lupus, (1998) Vol. 7, No. SUPPL. 2, pp. S103-S106.
 Meeting Info.: 8th International Symposium on Antiphospholipid Antibodies
 Sapporo, Japan October 6-9, 1998
 ISSN: 0961-2033.
 DT Conference
 LA English
 CC Immunology and Immunochemistry - General; Methods *34502
 Biochemical Studies - General *10060
 Blood, Blood-Forming Organs and Body Fluids - General; Methods
 *15001
 General Biology - Symposia, Transactions and Proceedings of Conferences,
 Congresses, Review Annuals *00520

BC Hominidae 86215

IT Major Concepts
 Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport
 and Circulation); Immune System (Chemical Coordination and Homeostasis)

IT Chemicals & Biochemicals
 beta-2-glycoprotein 1: plasma; lupus anticoagulants:
 beta-2-glycoprotein 1-dependence, prothrombin cofactor-dependence,
 subtypes; prothrombin: plasma

IT Miscellaneous Descriptors
 activated partial thromboplastin time: clotting test; dilute
 Russell's viper venom time: clotting test;
 kaolin clotting time: clotting test; Meeting Abstract; Meeting Paper

ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
 human (Hominidae): patient

ORGN Organism Superterms
 Animals; Chordates; Humans; Mammals; Primates; Vertebrates

RN 9001-26-7 (PROTHROMBIN)
 9002-05-5Q (THROMBOPLASTIN)
 9035-58-9Q (THROMBOPLASTIN)
 72162-96-0Q (THROMBOPLASTIN)

L109 ANSWER 4 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 1998:60955 BIOSIS
 DN PREV199800060955

TI Sensitivity of **Russells viper venom** tests to
factor VIII inhibitors.

AU **Exner, T.**; Dickeson, L. E.

CS Gradipore Res. Lab., North Ryde, NSW 2113, Sydney Australia

SO Blood, (Nov. 15, 1997) Vol. 90, No. 10 SUPPL. 1 PART 2, pp. 93B.
Meeting Info.: Thirty-ninth Annual Meeting of the American Society of
Hematology San Diego, California, USA December 5-9, 1997 The American
Society of Hematology
. ISSN: 0006-4971.

DT Conference

LA English

CC **Blood, Blood-Forming Organs and Body Fluids - General; Methods**
***15001**
Biochemical Studies - General *10060
Biophysics - General Biophysical Studies *10502
General Biology - Symposia, Transactions and Proceedings of Conferences,
Congresses, Review Annuals *00520

BC Hominidae 86215

IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport
and Circulation)

IT Diseases
hemophilia: blood and lymphatic disease, genetic disease

IT Chemicals & Biochemicals
factor VIII inhibitors: discrimination; lupus anticoagulants:
discrimination

IT Methods & Equipment
Russells viper venom-based clotting test:
determination method, sensitivity

IT Miscellaneous Descriptors
Meeting Abstract

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae): patient

ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

RN 9001-27-8Q (FACTOR VIII)
109319-16-6Q (FACTOR VIII)
113189-02-9Q (FACTOR VIII)

L109 ANSWER 5 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1995:505111 BIOSIS

DN **PREV199598510161**

TI Diagnostic methodologies for circulating anticoagulants.

AU **Exner, Thomas**

CS GRADIPORE, Riverside Corp. Park, 35-105 Delhi Rd., PO Box 1865, Macquarie
Cent., North Ryde 2113 Australia

SO Thrombosis and Haemostasis, (1995) Vol. 74, No. 1, pp. 338-344.
ISSN: 0340-6245.

DT General Review

LA English

CC Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biochemical Studies - Lipids 10066
Biochemical Studies - Carbohydrates *10068
Pathology, General and Miscellaneous - Diagnostic *12504
Metabolism - Carbohydrates *13004
Metabolism - Proteins, Peptides and Amino Acids *13012
Cardiovascular System - Blood Vessel Pathology *14508
Blood, Blood-Forming Organs and Body Fluids - General; Methods
***15001**
Blood, Blood-Forming Organs and Body Fluids - Blood and Lymph Studies
***15002**

Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and
Reticuloendothelial Pathologies *15006
Reproductive System - Pathology *16506

BC Hominidae *86215

IT Major Concepts

Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cardiovascular Medicine (Human Medicine, Medical Sciences); Hematology (Human Medicine, Medical Sciences); Metabolism; Pathology; Reproductive System (Reproduction)

IT Chemicals & Biochemicals

THROMBOPLASTIN

IT Miscellaneous Descriptors

ACQUIRED THROMBOTIC DISORDER; ACTIVATED PARTIAL THROMBOPLASTIN TIME; DILUTE RUSSELL'S VIPER VENOM TIME; KAOLIN CLOTTING TIME; PHOSPHOLIPID-INTERFERING ANTIBODY; RECALCIFICATION CLOTTING TIME; RECURRENT SPONTANEOUS ABORTION; TEXATRIN AND TAIPAN VENOM TEST; TISSUE THROMBOPLASTIN INHIBITION TEST

ORGN Super Taxa

Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name

human (Hominidae)

ORGN Organism Superterms

animals; chordates; humans; mammals; primates; vertebrates

RN 9002-05-5Q (THROMBOPLASTIN)

9035-58-9Q (THROMBOPLASTIN)

72162-96-0Q (THROMBOPLASTIN)

L109 ANSWER 6 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1994:310535 BIOSIS

DN PREV199497323535

TI Some recent developments with lupus anticoagulants.

AU Exner, T.

CS Haemostasis Reference Lab., Westmead Hosp., Sydney, NSW 2145 Australia

SO Blood Coagulation & Fibrinolysis, (1994) Vol. 5, No. 2, pp. 281-289.
ISSN: 0957-5235.

DT General Review

LA English

AB Lupus anticoagulants (LA) have been defined as phospholipid-interfering antibodies. Testing for them has become a frequently requested procedure in coagulation laboratories and new methods have recently become available. Activated partial thromboplastin time (aPTT) reagents with reduced levels or different types of phospholipid provide high sensitivity. Correction procedures resistant to heparin and based on aPTT and dilute Russell's viper venom time (DRVVT) tests with added hexagonal phase phospholipids have improved the specificity of testing. Simplified tests based on venom activators of factor X and prothrombin improve the reliability of LA testing and may facilitate the further categorization of circulating anticoagulants. Recent studies on the mechanism of LA derived from various patients have confirmed their heterogeneity, principally in the protein cofactors involved in their interactions with phospholipids. Perhaps one-third of LA require beta-2-glycoprotein 1 to exert an anticoagulant effect. The remainder may require human prothrombin as suggested from studies with reconstituted clotting factor systems.

CC Biochemical Studies - Proteins, Peptides and Amino Acids 10064

Biochemical Studies - Carbohydrates 10068

Metabolism - Carbohydrates *13004

Metabolism - Proteins, Peptides and Amino Acids *13012

Blood, Blood-Forming Organs and Body Fluids - Blood and Lymph Studies *15002

Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and Reticuloendothelial Pathologies *15006

BC Hominidae *86215

IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Hematology (Human
Medicine, Medical Sciences); Metabolism
IT Miscellaneous Descriptors
ANTIPHOSPHOLIPID ANTIBODY; THROMBOSIS
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates

=> d his

(FILE 'HOME' ENTERED AT 07:32:18 ON 13 MAY 2002)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 07:32:46 ON 13 MAY 2002

E PROTEIN C/CN
L1 1 S E3
E ACTIVATED PROTEIN C/CN
L2 1 S E3
E BLOOD-COAGULATION FOACTOR XA/CN
E BLOOD-COAGULATION FACTOR XA/CN
L3 1 S E3
E ANTITHROMBIN III/CN
L4 1 S E3
E HEPARIN COFACTOR 2/CN
L5 1 S E6
L6 2 S 9000-94-6/CRN
L7 1 S 81604-65-1/CRN
L8 1 S L6 AND L7
E BLOOD-COAGULATION FACTOR X/CN
L9 1 S E3
E PROTHROMBIN/CN
L10 1 S E3
E THROMBIN/CN
L11 1 S E3
E BLOOD-COAGULATION FACTOR V/CN
L12 1 S E3
L13 2 S (HEPARIN OR HEPARIN, SODIUM SALT)/CN
L14 1 S DERMATAN/CN
L15 1 S DEXTRAN SULPHATE/CN

FILE 'HCAPLUS' ENTERED AT 07:39:58 ON 13 MAY 2002

E EXNER T/AU
L16 54 S E3-E5
E GRADIPORE/PA,CS
L17 33 S E3-E18
L18 80 S L16,L17
E OW99-AU69/AP,PRN
E WO99-AU69/AP,PRN
L19 1 S E3,E4
L20 1 S L18 AND L19

FILE 'REGISTRY' ENTERED AT 07:44:29 ON 13 MAY 2002

L21 1 S 14127-61-8
L22 1 S 28728-55-4
L23 1 S 166799-93-5

FILE 'HCAPLUS' ENTERED AT 07:45:52 ON 13 MAY 2002
E VENOM/CW

L24 9457 S E4
 E VENOM/CT
 E E7+ALL
 L25 9273 S E3+NT
 L26 19658 S E3,E5/BI
 L27 7518 S SNAKE (L) VENOM?
 L28 19690 S L24-L27
 E AGKISTRODON/CT
 E E3+ALL
 L29 518 S E6+NT
 L30 1268 S E6-E27/BI
 E AGKISTRODON
 L31 1277 S E1-E14
 L32 243 S (AGKISTRO? OR A) () (CONTORTRIX OR PISCOVOR? OR BILINEAT? OR MO
 L33 227 S AGKISTRO? (L) (CONTORTRIX OR PISCOVOR? OR BILINEAT? OR MOCCAS
 L34 19855 S L28-L33
 E VIPER/CT
 E E4+ALL
 L35 2 S E3,E4
 E E28+ALL
 L36 262 S E7+NT
 L37 369 S E7-E12/BI
 E E6+ALL
 L38 615 S E6+NT
 L39 1124 S E6-E35/BI
 E VIPER
 L40 2387 S E3,E4,E7,E8,E9,E10,E11
 L41 447 S E13-E17,E22,E23,E24
 E NOTECHIS/CW
 L42 104 S E3
 E NOTECHIS/CT
 E E3+ALL
 L43 104 S E6+NT
 L44 162 S E6-E17/BI
 E PSEUDONAJA/CT
 E E3+ALL
 L45 38 S E6+NT
 L46 54 S E6-E12/BI
 E OXYURANUS/CT
 E E5+ALL
 L47 77 S E6+NT
 L48 122 S E6-E10/BI
 L49 20335 S L34-L48
 L50 976 S RUSSEL? (L) (SNAKE OR VIPER?)
 L51 156 S COPPERHEAD OR COPPER HEAD
 L52 20373 S L49-L51
 L53 11 S L18 AND L52
 E BLOOD COAGULATION/CT
 E E3+ALL
 L54 12573 S E7+NT
 E BLOOD CLOT/CT
 E E6+ALL
 L55 483 S L52 AND L54
 L56 2295 S L52 AND (?COAGUL? OR CLOT?)
 L57 2295 S L55,L56
 L58 168 S L52 AND (L1 OR PROTEIN C OR FACTOR XIV)
 L59 158 S L52 AND (L2 OR PROTEIN C (L) ACTIV? OR FACTOR XIVA)
 L60 157 S L58 AND L59
 L61 42 S L60 AND (L3 OR FACTOR XA OR FACTOR X(L)ACTIV?)
 L62 0 S L60 AND L8
 L63 1 S L8
 L64 1 S L60 AND (L4 OR ANTITHROMBIN III) AND (L5 OR HEPARIN (L) COFAC
 L65 103 S L60 AND (L9 OR FACTOR X OR L10 OR PROTHROMBIN OR FACTOR II OR

L66 24 S L60 AND (L21 OR CALCIUM(L)ION OR CA2# OR CA(L)ION)
 L67 19 S L60 AND (L13 OR L14 OR L15 OR HEPARIN OR DERMATAN OR DEXTRAN(
 L68 18 S L60 AND (L23 OR FACTOR(L)V (L) LEIDEN)
 L69 76 S L61,L66-L68
 L70 62 S L69 AND L65
 L71 22 S L70 AND 9/SC
 L72 16 S L69 AND BLOOD ANALYSIS/CT
 L73 8 S L71 AND L72
 L74 8 S L73 AND L24-L73
 SEL DN 3 5 6
 L75 5 S L74 NOT E1-E3
 L76 128 S L60 AND (PD<=19980202 OR PRD<=19980202 OR AD<=19980202)
 L77 29 S L76 AND (BIOCHEM?(L)METHOD?)/SC,SX
 L78 26 S L77 AND L61-L75
 L79 68 S L76 AND L61-L75 NOT L77
 L80 17 S L79 AND (SCREENING OR KIT OR FUNCTIONAL ASSAY OR COMPARISON O
 L81 2 S L79 AND PROTAC/TI
 L82 6 S L79 AND BLOOD ANALYSIS/CT
 SEL DN 5 6
 L83 4 S L82 NOT E4-E5
 L84 13 S L80 NOT L81-L83
 SEL DN 3 7 12 13
 L85 9 S L84 NOT E6-E9
 L86 31 S L20,L53,L63,L64,L75,L81,L83,L85
 L87 59 S L69 AND L76
 L88 46 S L87 NOT L86
 SEL DN 4 6 9 15 23 27 28 38 39
 L89 9 S L88 AND E10-E18
 L90 18 S L85,L89
 L91 29 S L53,L90
 L92 29 S L91 AND (?COAGUL? OR CLOT? OR FACTOR OR BLOOD OR PLASMA OR SE
 L93 11 S L91 AND (RUSSEL? OR VIPER? OR PSEUDON? OR TEXTIL? OR NOTECH?
 L94 29 S L92,L93 AND L16-L20,L24-L93
 SEL DN 20
 L95 28 S L94 NOT E19

FILE 'HCAPLUS' ENTERED AT 09:33:59 ON 13 MAY 2002

SET COST ON
 SET COST OFF

FILE 'BIOSIS' ENTERED AT 09:35:51 ON 13 MAY 2002

E EXNER T/AU

L96 111 S E3,E4,E7,E8
 L97 21433 S L26 OR L27 OR L30 OR L31 OR L32 OR L33 OR L37 OR L39 OR L40
 L98 15 S L96 AND L97
 L99 13 S 150?/CC AND L98
 L100 13 S L98 AND PY<=1998
 L101 11 S L99 AND L100
 L102 101 S L96 NOT ARTICLE/DT
 L103 2 S L102 AND PATENT/DT
 L104 99 S L102 NOT L103
 L105 10 S L101 AND L104
 L106 12 S L103,L105
 L107 5 S L98 NOT L106
 SEL DN L106 1-6
 L108 6 S L106 AND E1-E6
 L109 6 S L103,L108

FILE 'BIOSIS' ENTERED AT 09:48:20 ON 13 MAY 2002